BRAIN DEVELOPMENT FROM SENSORIMOTOR EXPERIENCES: HANDWRITING AND LETTER PERCEPTION

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BRAIN DEVELOPMENT FROM SENSORIMOTOR EXPERIENCES:

HANDWRITING AND LETTER PERCEPTION

Handwriting is a visual-motor activity that is particularly effective at increasing letter recognition, a fundamental skill in early reading development. This dissertation focuses on understanding the neural mechanisms that underlie increases in letter recognition after handwriting practice. The hypotheses of this dissertation are that (1) the visual-motor coordination inherent to handwriting letters contributes to the emergence of coordinated neural activity among visual and motor brain systems during letter perception and that (2) the emergence of this visual-motor functional connectivity during perception translates to gains in visual letter recognition. In the first and second studies, I demonstrate that visual-motor functional connectivity supports handwriting in literate adults and that handwriting practice leads to a similar neural response during letter perception in preliterate children. In the third study, I demonstrate that the neural systems supporting letter perception in literate children primarily incorporate the visual system while those that support letter perception in adults incorporate both visual and motor systems. In the final study, I demonstrate that the contingency between the motor experience of handwriting and the visual experience of the letter as it is being produced contributes to increases in letter recognition with a temporary increase in visual-motor functional connectivity. These studies suggest, collectively, that one way that handwriting increases letter recognition is by establishing functional pathways among visual and motor brain systems that facilitate the influence of both visual and motor information during recognition. This research suggests, more broadly, that actions that tightly couple visual and motor systems are supported by functional connections that mold the neural mechanisms underlying object recognition.

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CHAPTER 1:

INTRODUCTION

Several theories of human development are based on the proposition that the reciprocity between action and perception is fundamental to developmental changes in cognition (Gibson EJ, 1988; Gibson JJ, 1966, 1979; Gottlieb, 1991, 2007; Lockman, 2000; Mareschal, 2007; Piaget, 1952, 1954; Thelen & Smith, 1994). A large number of studies have highlighted the importance of this reciprocity for cognitive development by demonstrating that it can give rise to behaviors that indicate a change in 'knowledge' (e.g., Bertenthal & Campos, 1990; Bertenthal & Von Hofsten, 1998; Bremner & Bryant, 1977; Bushnell & Boudreau, 1993; Horobin & Acredolo, 1986; Needham, 2000; Needham & Baillargeon, 1998; Rovee-Collier, Sullivan, Enright, Lucas, & Fagan, 1980; Rovee & Rovee, 1969; von Hofsten & Fazel-Zandy, 1984). Visual proprioception, the sense of self-movement based on visual input (Gibson JJ, 1966, 1979), for instance, is heavily influenced by crawling experience and the co-development of these two processes leads to an apparent fear of heights (Bertenthal & Campos, 1990). Perception and action systems are, in essence, linked to each other through the interactions a learner has with their environment, continually changing what the learner does and perceives.

The main objective of this dissertation is to investigate a potential neural mechanism by which the linking between perception and action contributes to cognitive development. It proposes that actions with objects coordinate visual-perceptual, visual-motor, and motor activity in the brain and that this neural linking is a part of how objects are perceived and recognized. Actions that explicitly couple visual and motor systems would, therefore, coordinate neural activity among visual and motor brain systems. This visual-motor functional connectivity would contribute to the development of neural systems that support visual perceptual processes with those objects. Letter production, the creation of a single letter by hand, presents a unique opportunity to study the interaction between perception and action because it is an action that appears to necessitate both visual-perceptual and visual-motor guidance.

In what follows, I first review the literature related to the use of visual perceptual guidance in object manipulation and letter production through behavioral work in order to highlight the necessity for

perceptual knowledge in object-related actions. I will then briefly introduce letter production as an activity that requires not only perceptual knowledge about letters, but also the efficient integration among visual-perceptual, visual-motor, and motor processes. I will then explain the need for neuroimaging work that approaches letter production as a visual-motor behavior before delving into the neural systems that have been associated with letter production and perception in literate adults. I will then present what is known about the development of the neural systems that support letter production and perception, suggesting that these two systems develop together and may, in fact, rely upon the same functional network. There has, to date, been no studies of letter production and perception to assess the presence of such a functional network. I, therefore, review the small amount of literature that exists on the development of functional connectivity between sensory and motor systems and the relevance of such functional connections to learning more broadly.

Visual Perceptual Guidance During Object Manipulation

The mechanisms by which the perception-action loop changes what a learner does and perceives have been extensively studied in the domains of visual object recognition and object-directed action (e.g., Needham, 2000; Rovee-Collier et al., 1980; von Hofsten & Fazel-Zandy, 1984). These domains of research include work that has focused on the role of action in the development of visual object recognition (e.g., Harman, Humphreys, & Goodale, 1999; James, Humphreys, Vilis, Corie, Baddour, & Goodale, 2002; Craddock, Martinovic, & Lawson, 2011; James, Jones, Swain, Pereira, & Smith, 2014). This literature suggests, in general, that actions with objects create visual inputs that increase visual recognition. Planar views, for instance, are particularly helpful views for learning to visually recognize an object and occur more often than chance during spontaneous object exploration (James, Jones, Smith, & Swain, 2014). Object-directed actions, essentially, provide the learner with visual input that is conducive to the development of visual object recognition.

The structure of the human body provides some gross structure of object views while other mechanisms provide more nuanced object views—both levels appear to be geared towards increasing the learner's ability to visually recognize the object in the future. Humans have two hands, for instance, and

holding an object with both hands brings that object to the center of view where it is more likely to be fixated and remembered when named (Pereira, Smith, & Yu, 2014; Yu & Smith, 2013). Within the bounds of such anatomical influences, the fine motor system can provide more nuanced views of objects through manual manipulation, such as rotating the object. Rotating objects increases a learner's ability to recognize those objects (Harman et al., 1999), perhaps due to the prevalence of planar views in such rotations (James et al., 2002; James et al., 2014).

There is evidence to suggest that the structuring of object views by the fine motor system is guided by the visual perceptual system at some level. The bias to present oneself with planar views persists even without direct hand-to-object contact, for instance. When asked to learn objects presented in a virtual environment, adults still demonstrated a clear bias towards planar views even though they were only able to rotate the objects virtually (Harman et al., 1999; James, Humphrey, & Goodale, 2001; James et al., 2002). Children demonstrated a similar bias when manually exploring novel objects fixed within a clear sphere (James et al., 2014). These studies demonstrate that constraints related to the interaction between the structure of the human body and object shape or tactile preferences for object exploration cannot account for the bias towards planar views. They demonstrate that the motor system can structure visual input based upon purely visual cues and, furthermore, that the bias towards planar views is a preference of the *visual* perceptual system.

Several lines of evidence have suggested that the preferences of the visual system are specific to each learner—that they develop through experience. While the visual system may develop similar preferences among humans (e.g., planar views), it may also develop individual preferences. Self-guided object exploration results in greater recognition gains than other-guided exploration, for instance, even when the prevalence of planar views and other views that facilitate recognition are equated (James et al, 2002). Even in cases where the object is not allowed to rotate, as in the case of aperture-viewing, self-guided exploration results in greater gains than other-guided exploration (Craddock et al., 2011). That these individual preferences develop and change through experience is demonstrated by the finding that there was no recognition benefit from viewing one's own past visual experience relative to the visual

experience of another (Craddock et al., 2011). These findings, together, suggest that each interaction a learner has with an object contributes to an ongoing process of perceptual refinement that is largely guided by the current status of the developing perceptual representation.

The impact of developing perceptual representations on fine motor movement is most evident when a learner creates objects themselves because the object they create is, presumably, matched to that learner's perceptual representation of that object. Work in this line of investigation has focused on drawing tasks that ask participants to recreate two-dimensional forms using pen and paper. Drawings from one object category (e.g., cow) become recognizably distinct from drawings of another category (e.g., horse) as adult learners gain experience drawing those forms (Fan, Yamins, & Turk-Browne, 2017). A similar progression can be seen in children who are just learning to write letters of the alphabet. With practice, letters from one category (e.g., G) become recognizably distinct from letters of another category (e.g., C). Drawing practice leads to the production of more accurate forms and, at the same time, leads to more accurate recognition for the practiced forms compared to practicing other motor movements, such as typing (Longcamp, Zerbato-Poudou, & Velay, 2005). In the context of the work discussed above, these finding suggest that the fine motor system creates forms that are particularly conducive to learning to visually recognize them while at the same time changing the fine motor movements to match the developing perceptual representation.

This phenomenon—increasingly recognizable hand-drawn forms with practice—cannot be explained by increases in motor skill alone. Young children between the ages of 6 and 12, for instance, typically demonstrate difficulty in copying the Rey-Osterreith Complex Figure. When asked to reproduce individual parts of the complex form, however, their copying performance increased, suggesting that the complexity of the figure leads to copying errors and not an inability of the fine motor system to reproduce it by hand (Akshoomoff & Stiles, 1995). A similar complexity effect has been found for writing letters of the alphabet by hand in preschool children (Duval, Remi, Plamondon, Vaillant, & O'Reilly, 2015). There is also work demonstrating that visual-only training can lead to more accurate copying than other training experiences, such as finger tracing (Vinter & Chartrel, 2008) or even direct experience copying the form

(Waber, Bernstein, & Merola, 1989). Such works provide support for the proposition that increases in the accuracy of forms produced by hand cannot be explained by increases in motor skill alone and point, again, to the influence of individual perceptual preferences on action and the ability of the fine motor system to match those preferences.

Visual and Motor Components of Letter Production

The ease with which literate adults write individual letters may falsely present letter production as a simple task—as a simple motor movement of the hand. Letter production is, in reality, a relatively complex sensorimotor behavior that involves several motor and sensory processes as well as perceptual guidance. Motor processes involved with letter production include fine-motor movements with the fingers, hands, and wrists as they manipulate a writing utensil as well as eye-movements, postural control, head movements, and arm movements, to name a few (Feder & Majnemer, 2007; Trieman & Kessler, 2014). Arguments could be made for the involvement of all sensory systems during letter production though the sensations that accompany letter production are often thought to be dominated by somatosensation and vision (Feder & Majnemer, 2007; Trieman & Kessler, 2014). Somatosensation is inextricably bound to motor processes but vision has some room to vary; all movements are accompanied by somatosensations but not all movements are accompanied by visual inputs. I will, therefore, focus on the involvement of the sensory modality of vision in letter production and will characterize letter production more specifically as a complex *visual*-motor behavior.

In what follows, I coarsely delineate letter production into what I will call 'components' of letter production to provide a characterization of letter production as a visual-motor activity. These components include motor, visual-motor, and visual-perceptual and are meant to capture relatively distinct aspects of the many processes that may support letter production, making no claims of modularity. Motor processes include the processes associated with the actual execution of movement and necessarily include somatosensory processes. Motor processes can be guided by two distinct visual processes: visual-perceptual and visual-motor processes. Visual-perceptual guidance determines the shape and form of the letter to be written—the general plan for the action. Visual-motor guidance adjusts for the specifics of the

environment (e.g., the slant of the writing surface) while the motor plan is unfolding. These delineations are strongly-influenced by hypotheses concerning the complementary functions of the ventral and dorsal visual streams in visual-perceptual and visual-motor processes (Milner & Goodale, 1995; Ungerleider & Mishkin, 1982).

Motor component. The motor component of letter production is the actual execution of the motor movements required to create a letter through letter production and is dominated by the use of the fine-motor system to manipulate a writing utensil (Feder & Majnemer, 2007). The development of the fine-motor system is couched within the development of the gross-motor system and necessarily develops alongside sensory feedback (Cratty, 1979). Early in letter learning, for instance, motor process may be more heavily guided by sensory feedback than later in letter learning. Young children with very little writing experience experiment with pen grips and the many sensations that are created when pressing the pen to the paper and how to adjust their actions to create more desirable letterforms. The motor movements at this age are closer to letter copying—reproducing a letter form from an exemplar provided throughout the production episode (Tse, Thanapalan, & Chan, 2014). Later in learning, however, motor movements are closer to letter *production*—reproducing a letter form from one's own knowledge of the letter. Older children, who are by most measures literate and efficient at writing letters of the alphabet, create letters from their own knowledge of the letter forms, though the creation is still slow and 'messy' relative to adult letter production. At some point letter production becomes extremely efficient and relatively self-contained, requiring very little effort to quickly and consistently create legible letters. Adults can, for instance, produce legible forms based on somatosensory feedback alone while children, especially younger children, require the visual feedback as well (Maldarelli, Kahrs, Hunt, & Lockman, 2015; Fears & Lockman, 2018). At all stages the somatosensory feedback is integral to the execution of the movement, but the visual feedback is not integral at all stages. The motor component is, therefore, considered to include the actual execution of the movement as well as the use of somatosensory feedback in that execution.

Visual-motor component. Although the general movements required to produce a given letterform may be fairly standard across productions when knowledge of the letter form and motor plans are well-established, the actual force, velocity, and trajectory of each movement varies from one production to the next to account for specific environmental parameters (Wing & Nimmo-Smith, 1987; Longstaff & Heath, 1997). Guidance of the motor movement at this level is likely mediated by visual processes that support online motor guidance after the general motor plan has already been set in motion. Adults have very little awareness of the exact motor movements used with each letter production episode and the exact motor movements are instance-based with very little influence on future letter productions. Although adults can produce legible forms based on somatosensory feedback alone, their forms are produced with more ease and precision when visual feedback is provided (Zimmer, 1982). Knowledge of the letter form and the motor plan may only serve as rough guidelines for the production of the shape, leaving the in-the-moment production to real-time visual-motor guidance.

Visual-perceptual component. Visual-perceptual guidance during letter production is related to the explicit knowledge of a letter form and is likely associated with the formation of a motor plan in the early stages of letter learning and the selection of a motor plan in later stages. In young children, perceptual knowledge and motor plans are not well-established—this is a time when visual-perceptual knowledge is being formed. The visual experiences of a letter that are provided during letter production may have unique effects on the formation of visual-perceptual knowledge of letter forms at this age. The visual percepts produced by letter production include, in the least, the observation of the final handwritten letter, the stroke-by-stroke unfolding of the letter, and one's hand and pencil moving in time with the unfolding letter. As children gain experience with letters and perceptual knowledge becomes relatively well-established, it may begin to modulate the motor execution and, in doing so, begins to contribute to the formation of a motor plan. After an extensive amount of experience with letter production, the visual-perceptual knowledge and the motor plan should be consistent with one another. Visual-perceptual knowledge would, at this advanced stage, communicate directly with motor plans to guide action.

Methodological Considerations in Neuroimaging Studies of Letter Production

Most studies that have included letter production have typically used production as a test case for studying a related, but tangential phenomena. Production has been used to determine how the brain supports spelling (for review see Purcell, Turkeltaub, Eden, & Rapp, 2011), how parietal cortex modulates movement dynamics (e.g., velocity, turning, etc.; e.g., Seitz et al., 1997; Kadmon Harpaz, Flash, & Dinstein, 2014), and to determine the relationship between the neural systems supporting handwriting and those that support speech (Petrides, Alivisatos, & Evans, 1995; Brownsett & Wise, 2010), to give a few examples. The majority of studies that have included letter production have not focused on how the brain supports the action of letter production—the physical production of individual letters. A disinterest in letter production, specifically, coupled with the difficulty of introducing writing devices into the fMRI environment for flexible stimulus display have resulted in a variety of possible methods for studying letter production in the fMRI environment.

Methods for letter production in the fMRI environment vary in terms of writing surfaces, writing implements, and writing tasks. In terms of writing surfaces, adult participants have been asked to write in the air (Katanoda, Yoshikawa, & Sugishita, 2001; Omura, Tsukamoto, Kotani, Ohgami, & Yoshikawa., 2004; Sugihara, Kaminaga, & Sugishita, 2006), on a hard or paper writing surface by their waist (hard plastic or wood surface: Longcamp, Anton, Roth, & Velay, 2003; Nakamura et al., 2000; Nakamura, Ooi, & Yura, 2002, paper surface: Beeson et al., 2003; James & Gauthier, 2006; Roux et al., 2009; Rapp & Dufor, 2011; Segal & Petrides, 2012; Shah et al., 2013), or on a plastic handwriting recording device (Tam, Churchill, Strother, & Graham, 2011) with (Longcamp et al., 2014) or without projecting their written productions onto a mirror above their head (Kadmon Harpaz et al., 2014; Rektor, Rektorová, Mikl, Brázdil, & Krupa, 2006; Siebner et al., 2002). In terms of writing implements, adult participants have been asked to write with their finger (Katanoda et al., 2001; Omura et al., 2004; Sugihara et al., 2006), with a keyboard (Purcell et al., 2011), or with a pen or pencil (Beeson et al., 2003; Kadmon Harpaz et al., 2014; Longcamp et al., 2014; Nakamura et al., 2002; Roux et al., 2009), sometimes including a hand avatar in the image (Karimpoor et al., 2017). In terms of writing tasks, adult participants

have been asked to write letters in manuscript (James & Gauthier, 2006; Katanoda et al., 2001; Longcamp et al., 2003; Seitz et al., 1997; Tokunaga et al., 1999), generate and write words (Beeson et al., 2003; Katanoda et al., 2001; Petrides et al., 1995), spell words (Purcell et al., 2011), and generate narratives (Brownsett & Wise, 2010). Some studies have even asked participants to simply imagine writing (Harrington, Farias, Davis, & Buonocore, 2007; Tokunaga et al., 1999).

Very few of these methods have the ability to preserve any part of the visual-motor nature of letter production, however, and none of them allow participants to see their hand and the letter being created as they are writing on the surface onto which they are writing. The handwriting recording device developed in Tam et al. (2011) can be used to project participants' handwritten letters onto a mirror above their head—in real time as they are writing. This device allows participants to use visual feedback of the letter to guide their motor movements in real-time and presents the most ecologically valid method available for studying letter production as a complex visual-motor behavior in the fMRI environment.

Neural Systems Supporting Letter Production

Producing letters by hand is supported by a neural system that can be said to encompass motor, visual-motor, and visual-perceptual brain regions. Studies that studied letter production, specifically, have routinely reported that frontal, parietal, and ventral-temporal cortices were active (James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; Longcamp et al., 2008; Longcamp, Hlushchuk, & Hari, 2011; Longcamp et al., 2014; Seitz et al., 1997; Siebner et al., 2001; Planton, Jucla, Roux, & Démonet, 2013). Theories of two visual streams (Milner & Goodale, 1995; Ungerleider & Mishkin, 1982) would suggest that this neural system includes both ventral and dorsal visual streams in addition to motor cortex. These theories would suggest that each region within this distributed neural system would participate in letter production in a way that is coarsely distinguishable from the participation of the other regions. Motor processes would be associated with frontal motor regions and somatosensory regions in anterior parietal cortex. Dorsal visual stream regions would be associated with visual-motor processes in posterior parietal cortex. Ventral visual stream regions would be associated with visual-perceptual processes in ventral-temporal cortex. I, therefore, provide information on the

particularities of each region's function to impress the strong likelihood that these regions are differentially involved in the motor, visual-motor, and visual-perceptual components of letter production.

Motor: Frontal motor regions (left precentral gyrus, left superior and middle frontal gyri). Large bodies of work have documented the recruitment of motor regions in frontal cortex for action execution (for review: Schieber, 2001; Graziano, 2006; Meier, Aflalo, Kastner, & Graziano, 2008). Not surprisingly then, primary motor and premotor cortices have consistently been shown to be involved in the fine motor movements required during letter and word production (letters: James & Gauthier, 2006; Dufor & Rapp, 2013; Longcamp et al., 2014; Haar, Donchin, & Dinstein, 2015; words: Planton, Longcamp, Péran, Démonet, & Jucla, 2017; for meta-analyses of writing studies see Purcell et al., 2011 and Planton et al., 2013) and drawing shapes (James & Gauthier, 2006; Potgieser & de Jong, 2016; Planton et al., 2017; for a meta-analysis of drawing studies see Yuan & Brown, 2015). The roles of primary and premotor cortices in action execution differ to some degree, however.

Primary motor cortex is a functionally defined region that most often maps onto the precentral gyrus, with the left primary motor cortex being most involved in the execution of movement on the contralateral side of the body (for review see Chouinard & Paus, 2006). Even within letter production research, primary motor cortex is closely tied to the actual execution of the fine motor movements required to produce a written form. For instance, primary motor cortex is recruited when participants write letters (James & Gauthier, 2006; Longcamp et al., 2003, 2014), draw shapes (James & Gauthier, 2006), or draw other forms (Yuan & Brown, 2014). This is not surprising, given the role of primary motor cortex in all forms of action execution.

Premotor cortex, often separated into dorsal premotor cortex, including posterior portions of the superior frontal and middle frontal gyri, and ventral premotor cortex, including posterior portions of the inferior frontal gyri and anterior-ventral portions of the precentral gyri, appears to have a more complex role in form production. Dorsal and ventral premotor cortices participate in movement in different ways. For instance, the left dorsal premotor cortex is recruited during visually guided reach-to-grasp movements with the right hand (Budisavljevic et al., 2017), is associated with finger movement sequencing of the

right hand (Budisavljevic et al., 2017; Chouinard & Paus, 2006), and is recruited during letter and shape production by hand (James & Gauthier, 2006; Longcamp et al., 2003). Ventral premotor cortex, on the other hand, is associated with hand shaping for object manipulation (Budisavljevic et al., 2017) and is recruited more during letter production than during shape drawing (James & Gauthier, 2006).

Dorsal premotor cortex, often referred to as Exner's area (Anderson, Damasio, & Damasio, 1990; Exner, 1881; Longcamp et al., 2003; Planton et al., 2013), has historically received attention for being one of the more crucial regions for producing written forms by hand. It is routinely recruited during various text production (Brownsett & Wise, 2010; Katanoda et al., 2001; Longcamp et al., 2003; Purcell et al., 2011) and drawing (Yuan & Brown, 2015) tasks. The exact location of this region remains debatable, however. Dorsal premotor responses during letter production have been reported in the posterior middle frontal gyrus (Pattamadilok, Ponz, Planton, & Bonnard, 2016) as well as posterior to the superior frontal gyrus in the superior frontal sulcus (Planton et al., 2017) and are generally considered to be left-lateralized (Roux et al., 2009; Pattamadilok et al., 2016; Planton et al., 2017).

Some evidence suggests that left dorsal premotor cortex codes for serial processing of graphemic-motor correspondences (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009) and has more recently been referred to as the graphemic-motor frontal area (Planton et al., 2017). As such, left dorsal premotor responses found during letter production would be attributed to the translation of stored grapheme representations, a stored perceptual representation of the letter "a" for instance, into the series of motor movements required to reproduce the letter on paper using a writing utensil. The production episode is characterized by a step-wise reproduction of the letter—one stroke followed by another—until the form is completed. This proposal fits nicely with evidence suggesting that dorsal premotor regions are involved in the sequencing of finger movements required for letter production (James & Gauthier, 2006; Longcamp et al., 2003) and the influence of perceptual knowledge on the selection of motor plans (Milner & Goodale, 2008). Left dorsal premotor recruitment during letter production, however, may not be specific to letter or grapheme production, as it is also recruited during non-letter and non-grapheme

production tasks (James & Gauthier, 2006; Longcamp et al., 2003, 2014; Planton et al., 2017; Yuan & Brown, 2015).

Visual-motor: Parietal cortex (left post-central gyrus, left superior parietal lobe, bilateral intraparietal cortex). Activation in parietal cortex is routinely found during letter production, very often in left postcentral gyrus, left superior parietal lobule, and bilateral intraparietal sulci (James & Gauthier, 2006; Longcamp et al., 2014). Activity in the superior parietal lobule (SPL) and the intraparietal sulcus (IPS) has traditionally been associated with visual-motor transformations (Jackson & Husain, 2006; Ogawa & Inui, 2009; for review Buneo & Andersen, 2006) and visually guided action (Goodale & Milner, 2005; Milner & Goodale, 2006) and these regions may serve a similar purpose during letter production. Activity in parietal cortex that included these regions was observed when participants wrote letters (Kadmon Harpaz et al., 2014; Longcamp et al., 2014; Seitz et al., 1997), but also when participants wrote digits (Longcamp et al., 2014), wrote whole words (Planton et al., 2017), copied novel forms (Planton et al., 2017; Yuan & Brown, 2014), and even if they simply made marks (Haar et al., 2015; Yuan & Brown, 2014). Thus, parietal cortex may not be related to motor plans in the same way that the frontal motor system is but may be more related to in-the-moment visually guided action, communicating with the frontal cortex to potentially augment motor plans (Rizzolatti, Luppino, & Matelli, 1998).

There is some indication of a graded involvement of the IPS in the visual-motor and motor components of letter production. Studies have demonstrated that anterior IPS is more closely associated with motor component of letter production whereas more posterior IPS is more closely associated with the visual-motor component (Haar et al., 2015; Kadmon Harpaz et al., 2014). Activation in left anterior IPS during letter production is generally related to the specification of movement trajectories (Haar et al., 2015; Kadmon Harpaz et al., 2014). For instance, the pattern of activation in the left anterior IPS can be used to predict the letter produced by a participant (Kadmon Harpaz et al., 2014). Posterior IPS however, is more active when participants move their pen to a particular spatial location if they are provided visual feedback concerning the location of their cursor (Thaler & Gooodale, 2011) or the mark produced by the pen (Yuan & Brown, 2014) than if they are not given visual feedback. The more anterior regions of IPS,

then, may be more associated with the motor component of letter production, whereas posterior regions of IPS may be more important for the visual-motor integration that is required during the act of letter production.

Visual-perceptual: Ventral-temporal cortex (left fusiform gyrus). The ventral-temporal cortex and, more specifically, the left fusiform gyrus, has traditionally been associated with letter (James, James, Jobard, Wong, & Gauthier, 2005) and word processing (Cohen et al., 2000; Dehaene, Le Clec'H, Poline, Le Bihan, & Cohen, 2002). The left fusiform gyrus, however, is also more active during letter production than shape production, even without seeing the form produced (James & Gauthier, 2006; Longcamp et al., 2003). This apparent category specificity has led to the interpretation that the left fusiform gyrus is comprised of neural traces of prior experiences with letters (i.e., letter representations) that can be accessed in a bottom-up manner through visual perception and in a top-down manner during letter production (James & Gauthier, 2006; Longcamp et al., 2014). The left fusiform gyrus is, therefore, generally considered to have some degree of letter-specificity and to potentially act as a store for abstract information about letters used for object categorization (e.g., A vs. G vs. D) (Dehaene et al., 2001; Dehaene et al., 2004; Dufor & Rapp, 2013; Polk & Farah, 2002; Rothlein & Rapp, 2014).

The right fusiform gyrus, on the other hand, is sensitive to exemplar variation for common objects (Koutstaal et al., 2001), exemplar variation for whole word reading (Barton, Fox, Sekunova, & Iaria, 2010a; Barton et al., 2010b; Qiao et al., 2010), and exemplar variation for letters (e.g., *A* vs. A vs. A) (Barton et al., 2010b; Gauthier et al., 2000; Koutstaal et al., 2001). The right fusiform gyrus is, therefore, generally considered to be associated with the processing of *handwritten* letters because handwritten letters are variations from the stereotypical category exemplar of typed letters (Gauthier et al., 2000; although, see Longcamp et al., 2011). Handwritten letter perception may involve more than the perception of category variability, however, because handwritten letters contain information about the motor movements used to produce them that an observer readily perceives (Babcock & Freyd, 1988; Freyd, 1987; Kandel, Orliaguet, & Viviani, 2000; Orliaguet, Kandel, & Boë, 1997).

Neural Systems Supporting Letter Perception

A large number of studies have investigated the neural systems that support letter perception and, together, provide substantial evidence that both ventral-temporal (Cohen et al., 2003; Dehaene, Cohen, Sigmund, & Vinkier, 2005; Flowers et al., 2004; Garrett et al., 2000; James et al., 2005; Wong, Jobard, James, James, & Gauthier, 2009) and frontal motor (Dufor & Rapp, 2013; James & Gauthier, 2006; Planton et al., 2013; Haar et al., 2015; Longcamp et al., 2014; Planton et al., 2016; Potgeiser & Jong, 2016) cortices are recruited during the passive perception of individual typed letters. Activation in ventral-temporal cortex has traditionally been interpreted as activity associated with visual recognition (James & Gauthier, 2006; Longcamp et al., 2003, 2008, 2011). Activation of frontal motor cortex during visual letter perception has been shown in numerous paradigms (James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; Kersey & James, 2013; Longcamp et al., 2003, 2005, 2008; Wamain, Tallet, Zanone, & Longcamp, 2012) and has been interpreted as a reactivation of motor information that is used during visual perception.

Activation in parietal cortex, however, is not routinely found during letter perception in literate adults (James & Gauthier, 2006; James et al., 2005; Longcamp et al., 2003; Wong et al., 2009, but see James & Atwood, 2008; Cao et al., 2013), even for handwritten letters (Longcamp et al., 2011). It is more routinely found in training studies that look at changes in the neural response to symbols learned through different training modalities. Parietal cortex responds alongside ventral-temporal and frontal-motor cortices during the perception of manuscript letters learned through production in preliterate children (James & Engelhardt, 2012), cursive letters learned through production in preliterate children (Kersey & James, 2013), and novel pseudo-letters learned through production in literate adults (James & Atwood, 2008; Longcamp et al., 2008). Within-experiment letter production experience does seem to increase activation in parietal cortex during letter perception; however, it is unclear why parietal cortex is not routinely found during letter perception in literate adults.

Most studies that have investigated letter perception in literate adults and have focused on the neural response to typed letters in the ventral-temporal cortex (Cohen et al., 2003; Dehaene et al., 2005;

Flowers et al., 2004; Garrett et al., 2000; James et al., 2005; Wong et al., 2009). The neural response during typed letter perception in ventral-temporal cortex is often found in the fusiform gyri. It is typically strongest in the left hemisphere (Gauthier et al., 2000) and is distinctly anterior to activation associated with typed word perception (James et al., 2005). The response has been localized to the left fusiform gyrus by contrasting brain activation observed during the perception of typed Roman letters to objects (Joseph, Cerullo, Farley, Steinmetz, & Mier, 2006), noise (Joseph et al., 2006), typed shapes (James & Gauthier, 2006), typed digits (Flowers et al., 2004; James et al., 2005), typed Chinese characters (James et al., 2005), typed Korean characters (Pernet, Celsis, & Démonet, 2005), typed pseudoletters (Longcamp et al., 2005; Pernet et al., 2005), and, more commonly, to a fixation baseline (James & Atwood, 2008; Longcamp et al., 2003, 2011). The visual processing of letters in literate adults, therefore, has traditionally been associated with activation in the left anterior fusiform gyrus.

There is some evidence to suggest that the left and right fusiform gyri are performing different processes during letter perception. The response in the left fusiform gyrus has been associated with object categorization (e.g., A vs. G vs. D) while the response in the right fusiform has been associated with processing variations of a given category member, or exemplar variation (e.g., A vs. A vs. A) (Barton et al., 2010a; Gauthier et al., 2000; Koutstaal et al., 2001). The response to letters in the left fusiform gyrus correlates with letter recognition accuracy (Garrret et al., 2000). The right fusiform gyrus, on the other hand, is sensitive to exemplar variation for common objects (Koutstaal et al., 2001), exemplar variation for whole word reading (Barton et al., 2010a; Barton et al., 2010b; Qiao et al., 2010), and exemplar variation for letters (Gauthier et al., 2000). The perception of handwritten letters in literate adults, therefore, has traditionally been associated with activation in the right fusiform gyrus (although, see Longcamp et al., 2011).

Handwritten letter perception may also be qualitatively different than typed letter perception because handwritten letters are more visually similar to the visual percepts created during letter production than typed letters. There may be, then, unique influences of the visual experiences with handwritten letters that are produced during letter production. I will focus on four potential ways that

letters as they are produced through letter production might be processed differently than typed letters: (1) that letters unfold gradually during letter production, (2) that letters produced by hand may contain visual cues for motion, and (4) that the letters produced are produced by the self, reflecting some form of ownership. Below, I outline the potential roles of the dorsal and ventral visual systems for each of these four visual percepts that are created during letter production.

The potential roles of the dorsal stream in handwritten letter perception. Handwritten letters carry with them information about the motor movements used to produce them (Babcock & Freyd, 1988; Freyd, 1983a; Kandel et al., 2000; Orliaguet et al., 1997) and, having been produced by a human hand with a finite set of potential movements, have kinematic-based constraints in their form (Rosa, Perea, & Enneson, 2016). Movement cues, such as these, facilitate letter recognition (Orliaguet et al., 1997), particularly when the movement cues are congruent with the writing style of the observer (Freyd, 1983b). Handwritten letter perception is, therefore, distinct from the perception of typed letters (e.g., Gauthier et al., 2000, 2006; Li & James, 2016), because handwritten letters carry kinematic information that an observer readily perceives. As with the perception of a letter dynamically unfolding, the use of subtle movement cues based on kinematic information present in handwritten forms may be more related to processing in the dorsal visual stream, given its use of such visual cues to make real-time adjustments.

Dynamic unfolding. Children are typically taught to produce letters with particular stroke orders (i.e., for an "R" you must first produce the vertical line, then the curve, then the diagonal line), for instance, leading to the perception of a letter that unfolds over time, stroke by stroke, and in the same stroke order each time. A recent case study has demonstrated that these stroke orders are stored and can influence recognition processes though they are often masked by ceiling effects in literate adults (Schubert, Reilhac, & McCloskey, 2018). A patient with impaired letter recognition ability demonstrated higher recognition rates when presented with a letter dynamically unfolding as if being written relative to their recognition rates with static, typed letters and, further, improvements were greater for letters presented in a standard stroke order relative to a non-standard order (Schubert et al., 2018). The patient had suffered a left ventromedial occipitotemporal lesion with spared dorsal visual stream regions,

suggesting that the use of the stroke order to identify letters was supported by the dorsal visual stream. A similar stroke order effect has also been found in healthy adult participants who were trained with novel symbols. Recognition was faster and more accurate when symbols were presented unfolding in learned compared to unlearned stroke orders (Vinci-Booher, Sehgal, & James, in prep.). The use of dynamic information associated with a letter's typical stroke order may, therefore, be a part of the dorsally-mediated neural processes that underlie letter perception.

Ownership. Kinematic cues present in handwritten forms may be especially salient when one observes a handwritten letter that was produced by one's self, provided that the observer has established their 'own' stereotypical way of writing letters (i.e., motor plans). Although there remains considerable variability in letters produced by adults, even when produced by the same adult (Wing & Nimmo-Smith, 1987), individuals can readily distinguish their own handwritten letter trajectories from those of another, whether the trajectories were originally produced with visual feedback (Knoblich, Seigerschmidt, Flach, & Prinz, 2002) or without visual feedback (i.e., with their hand, pen, and paper occluded) (Knoblich & Prinz, 2001). In the process of learning novel pseudoletters, however, participants demonstrate no difference in accuracy or reaction time when making authorship judgements for the handwritten forms (Sawada, Doi, & Masataka, 2016), suggesting that the ability to distinguish one's own handwritten letters from another's is based on a long history of experience with one's own handwritten forms. Although their responses indicated no difference between self- and other-produced pseudoletters, ERP analyses revealed a difference in neural responses to self- and other-produced pseudoletters that was independent of familiarity effects (Sawada et al., 2016), suggesting that sensitivity to the kinematics of one's own productions can begin relatively quickly when learning new written forms, even before any changes in behavior can be measured. Processing of one's own kinematic cues may be more likely to be associated with the dorsal motor system response during letter perception than processing of another's kinematic cues, given the importance of such cues to the visual guidance that occurs during letter production and the history of one's own motor system and the handwritten forms produced by it.

The potential roles of the ventral stream in handwritten letter perception. Aside from the association of each percept with the involvement of the dorsal motor system during letter production, there are perceptual experiences that may uniquely affect the ventral-temporal cortex. For instance, the visual information created by letter production also results in exposure to category variability (Longstaff & Heath, 1997; Wing & Nimmo-Smith, 1987), a known driver of category learning (e.g., Perry, Samuelson, Malloy, & Schiffer, 2010; Twomey, Lush, Pearce, & Horst, 2014; Twomey, Ranson, & Horst, 2014). Producing letters by hand results in different perceptual instances of the same letter category. Each production of the letter 'R', for example, is quite visually different from one production to the next in young children. All of these productions are, nonetheless, still belong to the letter category of 'R'. Variable category instances produced during letter production may broaden the category, leading to enhanced letter recognition.

The variability present in the handwritten forms created during letter production may have effects on the development of the visual stream that are distinct from the effects on the dorsal visual stream. For instance, Li and James (2016) asked 5-year-old children to learn novel Greek symbols through training activities that differed in terms of the motor and visual experiences they were given with each symbol. Children who were exposed to variable exemplars of each Greek symbol category during training, such as a handwritten symbol produced by themselves or by another child or in typed symbols presented in different fonts, were better able to categorize the symbols than children who were not exposed to variability. There were, importantly, no differences between motor and non-motor conditions, indicating that letter production may have effects that are driven by the visual experience alone. Ventral-temporal cortex may, therefore, develop its response for well-learned letters based on prior visual experience with the variability inherent to the handwritten letters created during letter production and not based on the motor or visual-motor experiences, specifically. Letter production may simply be a natural and reliable way to present the visual perceptual system with category variability.

The Co-development of Brain Systems Supporting Letter Production and Letter Perception

The developmental trajectory of the neural system supporting letter perception suggests that the sensorimotor nature of letter production is important for the development of processes in motor, visual-motor, and visual-perceptual brain systems during letter perception (cf. Polk & Farrah, 1998). The perception of individual letters recruits left dorsal precentral gyrus in motor cortex, intra-parietal sulci in visual-motor regions, and fusiform gyri in visual-perceptual regions in preliterate children after they receive letter production training (James & Engelhardt, 2012). Though the literate adult response to letters does not typically include a parietal response, it does typically include activation in the fusiform gyri and frontal motor regions (James & Gauthier, 2006; Loncamp et al., 2003, 2005). These observations have led to the hypothesis that producing individual letters by hand contributes to the development of the neural system supporting adult-like letter perception (James & Engelhardt, 2012; James, 2017).

The nature of what is developing is not understood, however, as there have been only a small handful of studies on the development of the neural systems supporting letter perception and no studies on the development of neural systems supporting letter production. Some authors have suggested that letter production recruits a sensorimotor network that is reified with each letter production experience and increasingly integrates visual-perceptual regions in ventral-temporal cortex (James & Gauthier, 2006; Longcamp et al., 2008), a suggestion that is generally in line with theories of sensorimotor representation (McClelland, McNaughton, & O'Reilly, 1995; Versace, Labeye, Badard, &Rose, 2009). The neural systems that comprise this sensorimotor network become so integrated among themselves and with visual-perceptual processes through repeated letter production practice that the entire network is re-engaged if any of the neural systems receives stimulation. This hypothesis receives support from the finding that the same set of motor and visual-perceptual regions are active when literate adults visually perceive letters without any motor activity and when they produce letters without visual feedback (James & Gauthier, 2006).

Competing hypotheses to the sensorimotor network account of the co-development of brain systems supporting letter production and letter perception propose that the process is more of a process of

segregation than integration. Some authors have suggested that if such a sensorimotor network existed during letter production, the developmental effect would be a refinement of the processes happening in each of the neural systems that comprise the network (Amit & Brunel, 1995; Freeman, 1995; Makino, Hwang, Hedrick, & Komuyama, 2016). The sensorimotor network is, then, more of a developmental mechanism that fine-tunes local processes. The prediction that would be made from this hypothesis is that less and less of the entire network would be re-engaged as experience with letter production increases. This hypothesis is in line with theories of memory consolidation that suggest qualitative differences in the neural representation of short- and long-term memories (Aizawa, Inase, Mushiake, Shima, & Tanji, 1991; Dayan & Cohen, 2011; Frankland & Bontempi, 2005; Makino et al., 2016) as well as theories regarding the relevance of functional brain networks to more localized brain changes (Amit & Brunel, 1995; Freeman, 1995).

Still other authors have suggested that brain regions that respond during letter production and perception are not related to either the integration or segregation of a larger functional network because they need not belong to a larger network (Dehaene & Cohen, 2007; Nakamura et al., 2012). Such hypotheses are based on the idea that specific regions in the human cortex are innately predisposed to perform certain processes that do not necessarily rely on the functioning of other, spatially distant cortical regions (e.g., Downing, Jiang, Shuman, & Kanwisher, 1999; Kanwisher, McDermott, & Chun, 1997; Peleen & Downing, 2017). Experiences like letter production, then, tap into those processes and engender developmental changes in their functioning simply by inducing activation in them. The developmental effect is that the neural systems that support letter production early on become tuned by their own functioning and, quite simply, get better at that process the more they do it. This hypothesis has a difficult time, however, explaining the responses found in motor cortex during passive perception.

There are, therefore, at least three competing hypotheses concerning the co-development of brain systems that support letter production and letter perception. The first of these is that a sensorimotor network becomes more integrated as a consequence of letter production practice, predicting that letter perception provides little stimulation early in letter learning and stimulates the entire sensorimotor

network in a bottom-up fashion by stimulating the visual-perceptual representation once letters are well-learned. The second is that a sensorimotor network becomes more segregated as a consequence of letter production practice, predicting that letter perception stimulates the entire sensorimotor network early in letter learning and that letter perception stimulates the entire set of sensorimotor regions independently once letters are well-learned. The third is that sensory and motor regions develop relatively independently of one another, predicting that letter perception stimulates the entire set of sensory and motor regions independently and that the degree to which they are stimulated changes with experience. There is, at present, very little direct support for any of these hypotheses because there have been no studies that have measured functional connectivity during either letter production or letter perception.

Functional Connectivity and Learning

Functional connectivity has become a major part of how we understand brain function, yet we know very little about how functional connectivity develops and its role in learning. Sensorimotor learning activities are widely known to be stronger drivers of learning-related changes when compared to unimodal learning activities (see Shams & Seitz, 2008 for review) and theorists often credit this difference to the ability of sensorimotor activities to 'lock' sensory and motor experiences in space and time (e.g., Ballard, Hayhoe, Pook, & Rao, 1997; Barsalou, Simmons, Barbey, & Wilson, 2003; Damasio, 1989; Smith, 2005). Neuroimaging studies using different imaging modalities have demonstrated that the locking of sensory and motor experiences that occurs in sensorimotor learning does, indeed, correlate with a locking of motor and sensory activity in the brain (EEG: Andres et al., 1999; fMRI: Basset, Yang, Wymbs, & Grafton, 2015; MEG: Mathewson et al., 2012). These prior works have demonstrated that functional connectivity—a 'locking' of neural activity—arises between neural systems when they are coupled with one another through the external world, at least during the early stages of skill acquisition.

That correlated functioning among neural systems can lead to changes in future correlations among neural systems is, essentially, the principle of Hebbian learning. Hebbian learning is foundational to theories of experience-dependent brain changes. It proposes that neuronal connections undergo activity-dependent changes that lead to either an integration or a segregation effect. It has two basic

tenants: (1) When two neurons repeatedly fire in a coordinated manner, the connections between them are strengthened, effectively increasing the likelihood of firing together in the future. (2) When two neurons repeatedly fire in an uncoordinated manner, the connections between them weaken, effectively reducing the likelihood of firing together in the future (Hebb, 1949). Extensions of these basic tenants have been proposed that suggest that experiences leave behind a residue of reverberating activity that gradually decreases with time but continues, nonetheless, to change neuronal functioning (Hebb, 1949; Alvarez & Squire, 1994).

The principles of Hebbian learning would predict that behaviors that invoke a similar pattern of activation in different neural populations will increase the likelihood that these neural populations will display similar patterns of correlated activity in the future. The ability of self-generated actions to coordinate the activity in different neural systems may, therefore, have the ability to link motor, visual-motor, and visual-perceptual systems within a learner during a learning event. Other-generated actions have the ability to present the learner with various perceptual inputs but cannot generate the same coordinated neural activity within the learner because they are not performed by the learner themselves. Visual-motor coordination is, in this way, unique to self-generated actions and may correspond to a developmental mechanism by which the perceptual system establishes neural connectivity with the motor system, perhaps for the purpose of perceptual guidance for overlearned motor movements. If such a mechanism exists at the cortical level, it would lead to a sensorimotor functional network that is reflective of the learner's sensorimotor history and enriched for objects with which the learner has interacted.

Intrinsic functional connectivity and learning. A large amount of studies investigating training-induced changes in functional connectivity among cortical regions would, at first glance, appear to support the notion that sensorimotor experiences facilitate integration among sensory and motor systems (e.g., Albert, Roberson, & Miall, 2009; Astle, Barnes, Baker, Colclough, & Woolrich, 2015: Lefebvre et al., 2017; Taubert, Lohmann, Margulies, Villringer, & Ragert, 2011; Veroude, Norris, Shumskaya, Gullberg, & Indefrey, 2010). The vast majority of these studies come from measures of functional connectivity while participants are at rest, referred to as resting state functional connectivity.

Resting state functional connectivity is often used to assess the effects of experience on the intrinsic relationship among activity in different neural systems, referred to as intrinsic functional connectivity (for reviews see Buckner, Krienen, & Yeo, 2013; Van Den Heuvel & Pol, 010; Van Dijk et al., 2009). It has been found that a surprisingly small amount of training can induce changes in intrinsic functional connectivity (e.g., Veroude et al., 2010) and several more recent works have begun to try to understand the implications of these training-induced changes for human behavior (Ma, Narayana, Robin, Fox, & Xiong, 2011; Phillip & Frey, 2016; Sampaio-Baptista et al., 2014). These more recent works suggest that the trajectory is, surprisingly, more likely a trajectory of segregation.

The general approach to training-induced changes in intrinsic functional connectivity has been that the change is indicative of 'learning' and is, therefore, relatable to some change in behavior. When asked to listen to continuous speech in a novel language, participants who learned the most words demonstrated greater resting state functional connectivity among neural systems associated with phonological processing than participants who learned less words (Veroude et al., 2010), for instance. When training on a shape identification was restricted to one visual hemisphere, performance gains on the task and changes in resting state functional connectivity were positively correlated in the trained hemisphere but not in the non-trained hemisphere (Lewis, Baldassarre, Committeri, Romani, & Corbetta, 2009). Training-induced changes in intrinsic functional connectivity, therefore, appear to be related to measurable changes in behavior.

Several more recent studies have suggested that the magnitude and direction of training-induced changes in resting-state functional connectivity may be related to whether the learner is in the early or late stages of learning. Resting state functional connectivity is generally large and positive in the early stages of learning but small and, potentially, negative in later stages. Changes in resting state functional connectivity positively correlated with performance on a motor task until performance plateaued at which time resting state functional connectivity began to dissipate even as training continued (Ma et al., 2011). Changes in resting state functional connectivity positively correlated with performance on a juggling task after a short amount of training but was negatively correlated in participants whose training was more

intensive (Sampaio-Baptista et al., 2014), suggesting that more training led to less connectivity. These studies provide a more nuanced account of the association between intrinsic functional connectivity and learning, suggesting that intrinsic functional connectivity may be related to the neural mechanisms that support early learning.

A recent study has provided additional information concerning the role that intrinsic functional connectivity might play in the process of learning by investigating how long learning-related changes in intrinsic functional connectivity are maintained after training ends. Phillip and Frey (2016) measured intrinsic functional connectivity before training, after training, and again at a 6-month follow-up visit. Training occurred over the course of 10 days and consisted of a tracing task in which the participants were instructed to prioritize accuracy in their drawings. Resting state functional connectivity was greater after training and positively correlated with the fluency of their drawings. Performance on the drawing task was maintained at the 6-month follow-up visit and, somewhat surprisingly, the resting state functional connectivity was not. These results support the notion that increases in intrinsic functional connectivity are associated with learning but suggest that such changes may not be related to early learning processes alone but may also be related to the amount of time between the last training episode and the measurement of intrinsic functional connectivity. Indeed, other studies have reported similar trajectories: resting-state functional connectivity decreases monotonically after reading training ceases (Berns, Blaine, Prietula, & Pye, 2013).

In sum, intrinsic functional connectivity is greatest during the early stages of learning and immediately after training ceases. During early learning, it appears to positively correlate with behavioral measures of learning, suggesting that it is supporting the observed changes in behavior. That intrinsic functional connectivity decreases after training ceases would appear to suggest that training must occur regularly until learning plateaus to maintain the behavioral change. This is not the case, however. Intrinsic functional connectivity may decrease after training ceases, but the behavioral changes are maintained. Such findings are in line with theories that suggest that sensorimotor networks contribute to the

refinement of more localized processes or, at least, the refinement of other processes than the integration of the sensorimotor network itself (Amit & Brunel, 1995; Freeman, 1995).

Task-based functional connectivity and learning. Task-based functional connectivity studies provide additional information in that they can provide information concerning patterns of functional connectivity *during a task*. Training studies of task-based functional connectivity are nearly exclusively focused on assessing changes in functional connectivity during a task after *training on that task*. Work in this field is generally motivated by understanding the neural mechanisms that support early and late motor skill learning (for review see Makino et al., 2016) and has, therefore, placed special emphasis on the patterns of functional connectivity that support early learning compared to late learning. The task-based functional connectivity literature has demonstrated, in general, that changes in functional connectivity during a practiced task are related to changes in the ability to perform the task itself. Findings are similar to those in the intrinsic functional connectivity literature: performing a motor skill that is not well-learned corresponds to greater functional connectivity than performing well-learned motor skills.

Task-based functional connectivity displays the general trend toward less functional connectivity as learning increases and, furthermore, that functional connectivity during a task can be related to the modalities that would be expected to be relevant for the task (i.e., visual, somatosensory, motor, etc.). Functional connectivity among somatomotor and premotor regions, for instance, was greater while performing novel finger sequences compared to well-learned sequences (Sun, Miller, Rao, & D'Esposito, 2006). A similar pattern has been found among visual and motor regions for the learning of visually guided piano key sequences: early learning was characterized by stronger functional connections among primary visual and motor brain regions that were progressively less connected as skill in the performance of the piano sequences increased (Basset et al., 2015). When the task is purely visual, early learning is characterized by stronger functional connectivity among primary visual regions whether the training was focused on identifying affective stimuli (Damaraju, Huang, Barrett, & Pessoa, 2009) or visually-presented textures (Schwartz, Maquet, & Frith, 2002). These studies demonstrate that the communication among

neural regions that occurs during the performance of a task is related to the modalities required to perform that task and, further, that communication is greatest when the task is novel.

There is, to my knowledge, no work looking at the relationship between training and task-based functional connectivity during the performance of *a task other than the one that was trained.* Behavioral work has consistently demonstrated that training in one task can lead to performance gains on a second task (e.g., Longcamp, Zerbato-Poudou, & Velay, 2005; Zemlock, Vinci-Booher & James, 2018), but there is no work to demonstrate how this type of learning is related to neural changes supporting the second task. Training on letter production tasks might, for instance, lead to changes in the functional connections that support letter *perception*, as would be suggested by the sensorimotor network account of the co-development of brain systems supporting letter production and letter perception. Determining whether or not these changes correlate with changes in letter perception and the time course of these changes after training ceases will provide information concerning how the neural mechanisms that support early sensorimotor skill learning might translate to other, related tasks.

This Dissertation

Our understanding of brain function and human behavior is increasingly influenced by a growing body of knowledge concerning the degree to which distant neural systems in the brain coordinate their activity in the services of human behavior. Such coordination can be measured by estimating functional connectivity among neural systems in the brain (as suggested in Gazzaley, Rissman, & D'esposito, 2004; Voytek & Knight, 2015). Though the literature is replete with studies of functional connectivity, very few have investigated this phenomenon from a developmental perspective. We know very little about how functional connections develop and even less about the relationships among patterns of functional connectivity and learning-induced behavioral changes.

This dissertation uses letter production as an example of an activity that explicitly couples the motor, visual-motor, and visual-perceptual experiences of an object—a letter of the alphabet—that leads to gains in letter perceptual processing. Letter production is, therefore, a particularly useful example of a sensorimotor action that requires some perceptual guidance and translates to behavioral changes in

another, related process: visual letter recognition. Visual-perceptual systems may develop alongside the motor plans used to produce letters, eventually providing perceptual guidance of the motor movements. Visual-motor systems may also develop alongside motor plans but may be related more directly to the modulation of the motor movements to account for environmental peculiarities. Somatosensory and proprioceptive expectations of the motor plan are considered inseparable from motor execution processes and will, consequently be referred to collectively as the "motor" system. Visual-perceptual and visual-motor systems will be referred to collectively as the "visual" system, unless a more specific distinction of "visual-perceptual" or "visual-motor" is more appropriate.

This dissertation is comprised of five experiments that explore communication among visual and motor brain systems during letter production and subsequent letter perception with an emphasis on the perceptual process of recognition in the sensory modality of vision. The specific hypotheses of this dissertation are that (1) the visual-motor coordination inherent to letter production coordinates neural activity among visual and motor brain regions during letter production, that (2) this visual-motor coordination during letter production contributes to the emergence of visual-motor functional connectivity during letter perception, and that (3) the emergence of this visual-motor functional connectivity during perception supports gains in visual letter recognition.

The first experiment demonstrates that visual-motor functional connectivity supports letter perception in preliterate children, but only after experience with writing letters by hand and not after other motor experiences, such as typing (Chapter 2). The second and third experiments, together, demonstrate that letter production is supported by visual-motor functional connectivity but that literate letter perception is not (Chapters 3 and 4). The third experiment suggested that the visual and motor systems that respond during letter perception may develop their sensitivity to letters through different components of letter production and, therefore, not through the functional connectivity generated during letter production alone (Chapter 5). The final experiment manipulated the visual and motor contingencies of handwriting to determine the importance of the contingency between visual and motor experiences during

letter production to the neural mechanisms that support letter perception and to changes in letter recognition (Chapter 6).

The second, third, and fourth experiments described in this dissertation were conducted to address assumptions in the motivations behind Experiment 1 (Chapter 2). To conclude that visual-motor functional connectivity during letter perception was a re-engagement of the visual and motor systems that were used during letter production, we must also provide evidence for two additional claims. First, we must demonstrate that a visual-motor functional network supports letter production. Evidence in support of this claim is, therefore, presented in Chapters 3 and 4. Chapter 3 demonstrates that the neural system that supports letter production is coarsely separable into regions associated with the visual-perceptual, visual-motor, and motor experiences of letter production. Chapter 4 demonstrates that these visual and motor regions are functionally connected during letter production. Second, we must demonstrate that the visual-motor functional network that supports letter perception is similar to the network that supports letter production. We found, however, no evidence for this claim. Chapter 4 reports a null effect for several tests of functional connectivity during letter perception in adults, suggesting that while visual-motor functional connectivity supports letter production, it may not support literate letter perception.

The final chapter addresses two hypotheses generated by Experiment 1 (Chapter 2). The first of these hypotheses is that the visual-motor contingency inherent to letter production results in functional connectivity among visual and motor brain regions during perception. Chapter 6 provides support for this hypothesis: disjointed visual and motor experiences decouples visual and motor systems during letter perception in literate adults. The second of these hypotheses is that the emergence of visual-motor functional connectivity was related to gains in visual perceptual processes, specifically recognition. This proposal is complicated by the results reported in Chapter 4 that reported no evidence of functional connectivity during letter perception in literate adults. Chapter 6 provides support for the notion that functional connectivity may not support gains in visual recognition directly by demonstrating that gains in recognition following production practice persisted even as the functional connectivity patterns that accompanied the recognition gains faded.

CHAPTER 2:

VISUAL-MOTOR FUNCTIONAL CONNECTIVITY IN PRESCHOOL CHILDREN EMERGES AFTER LETTER PRODUCTION EXPERIENCE

An abundance of research has shown that the neural response associated with efficient letter recognition abilities in literate adults is characterized by activation in the ventral-temporal cortex during letter perception, particularly in the fusiform gyri (Cohen et al., 2003; Dehaene et al., 2005; Flowers et al., 2004; Garrett et al., 2000; James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; James et al., 2005, 2010; Kersey & James, 2013; Nakamura et al., 2012; Wong et al., 2009). Motor-oriented frontal regions are also active during letter perception, however, in addition to the fusiform visual perceptual regions (James & Gauthier, 2006; Longcamp, Tanskanen, & Hari, 2006). The involvement of these motor regions in letter processing is uncertain. It is unknown, for instance, if activity in motor cortex during letter perception is involved in perceptual processing or is, instead, independent of the visual perceptual processes so often associated with fusiform activity.

The evidence for and against the involvement of motor cortex in letter perception is correlational. Letter production, writing individual letters of the alphabet by hand, results in better letter recognition (Longcamp et al., 2005; Zemlock et al., 2018) and increased activation in motor regions of the brain (James & Engelhardt, 2012; Kersey & James, 2013) in preliterate children. Increased activity in motor regions of the brain, importantly, co-occur with increased activity in the fusiform gyri (James & Atwood, 2009; James & Engelhardt, 2012; Kersey & James, 2013) and activity in the fusiform gyri is related to letter recognition accuracy (Garrett et al., 2000). Gains in letter perceptual abilities after letter production, therefore, could be supported by activity in the fusiform gyri that is independent of motor cortex activity.

Several authors have posited that one reason that motor regions respond during letter perception is that early letter learning typically occurs through motor-oriented practice activities (e.g., letter production, tracing) (James & Gauthier, 2006; Longcamp et al., 2014). Activation of motor regions during perception is, then, thought of as a re-engagement of the regions used during learning. The set of motor regions that is active during letter perception is very similar to the set that is active during letter

production, for instance, with both including the left dorsal precentral gyrus (L dPrG), the left inferior frontal gyrus (L IFG), and the left middle frontal gyrus (L MFG) (James & Gauthier, 2006; Longcamp et al., 2014). The laterality of the frontal motor activations during letter perception is, furthermore, affected by handedness, with right handers demonstrating disproportionately large left motor activations and left handers demonstrating disproportionately large right motor activations (Longcamp et al., 2005). These studies, together, provide correlational evidence that motor brain regions respond during letter perception because they first responded during letter production but leave open the role that motor cortex might play in perception.

We propose that the engagement of both ventral-temporal and motor regions during letter perception is driven by the emergence of a functional network comprised of the neural systems that are used during letter production. We expect, in other words, that responses in ventral-temporal and motor brain regions during letter perception are not completely independent of each other—that they work together to support perceptual processes. Visual-motor training activities in which motor movements are closely tied to their perceptual output, as in the case of letter production, may facilitate the emergence of visual-motor communication pathways more than other visual-motor training activities, such as typing. Writing by hand requires the *formation of the letter form* using fine-motor skills and visual guidance, whereas typing requires a single button press to produce the complete desired form. We suspect that these putative functional connections between visual and motor brain regions become evident early in pre-literacy development as a function of experience with letter production.

If letter production experience creates functional communication pathways among visual and motor brain regions that come to support letter perception, then functional connectivity among these areas should be greater in preliterate children during letter perception after letter production practice than after other training experiences. This pattern of results would indicate that letter production couples visual and motor brain regions and that these regions work together during the subsequent perception of those letters. If, on the other hand, there is no evidence of functional connectivity among these regions during letter perception, then the recruitment of both visual and motor regions during letter perception reflects co-

activation due to chance, or experimental variables such as increased attention, heart rate, or responses to the physical environment of MRI. A robust method that provides information about task-based correlated functioning between regions that is present *in addition to* mere task-based co-activation is generalized psychophysiological interactions analysis, or gPPI (McLaren, Ries, Xu, & Johnson, 2012). We, therefore, used this method as described below.

Our goal in the present work, was to take the first step in directly addressing the issue of functional connectivity among visual and motor brain regions during letter *perception* after letter production practice. Here, we tested five specific hypotheses: First, training, in general, (letter production, tracing, typing), will result in greater functional connectivity between the fusiform gyri in ventral temporal cortex and widespread motor regions, including parietal and left frontal motor regions. Second, training, in general, would result in different functional connectivity patterns for letters than shapes. Third, different training conditions would result in different functional connectivity patterns. Fourth, functional connections between visual and frontal motor regions after training with letter production, specifically, would reflect the stimulus category: letter production will result in different functional connectivity patterns than shape production. Fifth, functional connections between visual and motor regions within the stimulus category of letters, specifically, would reflect the method of visual-motor training: letter production will result in greater functional connectivity among visual and frontal motor regions than letter tracing and letter typing.

Materials and Methods

All analyses were performed on a pre-existing data set that will be described here briefly and is presented in more detail in James and Engelhardt (2012).

Participants

Twenty preliterate 5-year-old children (8 females; ages 4:2 to 5:0) participated in this study; however, five children voluntarily withdrew before entering into the actual MRI environment, leaving the final sample size at 15 children. Per parental reports, all children were right-handed, preliterate, native English speakers with normal vision and normal neurological histories, free of any neurological trauma,

developmental disorders, and ongoing medication. In the gPPI analyses, data from five additional participants could not be used, resulting in data from 11 (6 females; ages 4:2 to 5:0) participants used in the present analysis.

Procedure

Participants were trained on different sets of letters and shapes through different types of visual-motor activity and then passively perceived those letters and shapes in a blocked design during fMRI scanning. The training, neuroimaging, and post-neuroimaging assessments all took place on the same day as part of the same visit.

Training. All children received the same three training conditions with letters and shapes. Children were asked to draw 4 letters and 4 shapes, 8 times each. The same children were then asked to trace a different set of 4 letters and 4 shapes, 8 times each. Finally, the children were asked to type a third set of 4 letters and 4 shapes, 8 times each (Figure 1). Letters included were 16 upper-case manuscript letters, presented in simple font style: B, F, G, A, Y, U, D, T, S, W, P, L, C, H, R, and K. Four letters were pseudo-randomly selected and distributed across three training conditions and one untrained condition. Shapes included flower, crescent, circle, parallelogram, leaf, rectangle, semicircle, triangle, star, raindrop, arrow, prism, clover, cylinder, pentagon, and ‘snowman’. The experimenter did not name any of the letters or shapes during any of the training conditions.

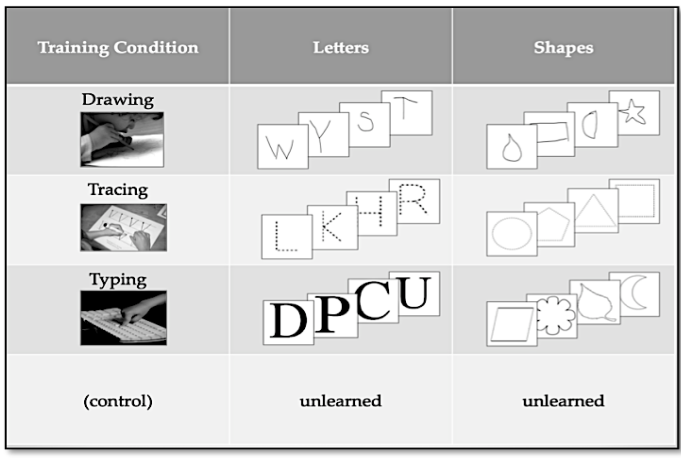

Figure 1. Experimental Conditions. Each child was exposed to different sets of letters and shapes through different sensorimotor training activities. An additional group of non-trained letters and non-trained shapes were also presented to them during the fMRI scanning session. For a particular child, a particular letter or shape appeared in only once of the four conditions.

Neuroimaging. After training, all children were first familiarized with the MRI environment by watching a cartoon in a full-sized mock scanner. Children then advanced to the actual MRI environment if both parent and child indicated that they were comfortable in doing so.

Stimulation protocol. All children underwent fMRI scanning while viewing the six different sets of trained stimuli and two additional sets of 4 letters and 4 shapes on which they were not trained (Figure 1). The children passively viewed these stimuli in a block design with each of the resulting 8 conditions being presented once per run. Each of the 8 blocks consisted of 16 stimuli from one of the conditions in a randomized order; thus, each stimulus was repeated 4 times within a block. Each stimulus was presented for 1 second with 0.5 seconds between stimulus presentations, resulting in 24- second blocks. Blocks were separated by a 10-second interval during which only a fixation cross was in view. The same fixation cross was also visible for 20 seconds at the beginning and end of each run. Each run was 4 minutes and 55 seconds long and 1-3 runs were collected per child depending upon their comfort level.

Scanning parameters. Neuroimaging was performed at the Indiana University Imaging Research Facility, housed within the Department of Psychological and Brain Sciences with a Siemens Magnetom TIM TRIO 3-T whole-body MRI system. A 12-channel phased array head coil was used. Children viewed the stimuli through a mirror in the bore of the scanner onto which a Mitsubishi XL30 projector displayed the stimuli. High-resolution T1-weighted anatomical volumes were acquired first using a Turbo-flash 3-D sequence: TI = 1100 ms, TE = 2.86 ms, TR = 1700 ms, flip angle = 12□, with 120 sagittal slices of 1.5 mm thickness and 0% slice gap, a field of view of 240 x 240 mm, and an isometric voxel size of 1.5 mm^3. For functional images, the field of view was 192 x 192 mm and 33 axial slices of 4.0 mm thickness were acquired with an in-plane matrix of 64 x 64 mm and 0% slice gap, producing a voxel size of 3.0 x 3.0 x 4.0 mm. Functional images were acquired using a gradient echo EPI sequence with interleaved slice order: TE = 30 ms, TR = 2000 ms, flip angle = 90º for blood-oxygen-level-dependent (BOLD) imaging.

Post-neuroimaging assessment. After scanning, children were tested to ensure their ability to identify the letters and shapes. Children also completed Phonemic Awareness, Letter Identification, and

Visual Word Discrimination subtests of the Bader Reading and Language Inventory (Bader, 2005) along with the Beery-Buktenica Developmental Test of Visual-motor Integration (Beery & Beery, 2006) to ensure equal pre-literacy among participants and characterize visual-motor skills, respectively.

Analyses

Functional connectivity analysis. To assess functional connectivity, we employed a generalized psychophysiological interactions (gPPI) analysis (McLaren et al., 2012). To perform a gPPI analysis, a design matrix is created that contains standard task predictors (*psycho*logical predictors), a predictor that is the activity of the seed region (*physio*logical predictor), and predictors for the interactions of task and seed (gPPI predictors). These predictors are entered into a mass univariate GLM model and applied to the functional data. One model is constructed for each seed region of interest. Therefore, one psychological predictor is entered for each task, one physiological predictor is entered for the seed, and one gPPI predictor is entered for each task. The psychological and physiological predictors are treated as predictors of no interest; their role as covariates is to account for changes in the BOLD signal that are purely driven by task or correlations between voxels that are purely driven by physiological noise. This is the key to the utility of the gPPI method to infer functional connectivity from brain activation measurements.

Each predictor type plays a very important role in the model. A psychological predictor exists for each task and these predictors absorb variance that is best explained by each task, which is similar to a standard GLM used to detect task-based activation. The physiological predictor, then, will absorb variance that is best explained by the activity of the seed region and, therefore, effectively represents the strength of correlation with the seed. However, the beta-weight assigned to the physiological predictor will correspond to the strength of the correlation with the seed that is non-task-specific, because the main task-based activation is already accounted for by the psychological predictors. Although important, the psychological and physiological predictors are essentially predictors of no interest. What is interpreted are the beta-weights assigned to each gPPI predictor, which, due to the presence of the psychological and physiological predictors in the model, represents the strength of the correlation with the seed that is task-specific. In other words, the gPPI predictors will receive beta-weights that are reflective of the amount of

variance that can be explained by the task *and* correlated activity with the seed region – *a task-based correlation with the seed*. Thus, with the main effects of external stimulation (task-based activation) and physiology (seed region activity) regressed out of the functional data, the gPPI predictors provide a clear picture of the task-based correlation between the seed region and all other voxels that exists above and beyond what would be expected from the task and non-task-specific physiological influences alone.

Preprocessing. All preprocessing steps were performed in BrainVoyager QX™ version 2.8.0. Preprocessing of functional data included slice scan time correction, 3-D motion correction using trilinear/sinc interpolation, and 3D Gaussian spatial blurring with a full-width-at-half-maximum of 6 mm. Temporal high-pass filtering was done using a voxel-wise GLM with predictors that include a Fourier basis set with a cut-off value of 2 sine/cosine pairs, which included a linear trend predictor. Individual anatomical volumes were normalized to Talairach space (Talairach & Tournoux, 1988). During normalization, functional data were re-sampled to an isometric voxel size of 3.0 mm^3. Coregistration of functional volumes to anatomical volumes was performed using a rigid body transformation.

Motion correction. Measures of functional connectivity have been shown to be sensitive to head motion, being particularly problematic for between-groups analyses (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012; Power et al., 2014; Satterthwaite et al., 2012; Satterthwaite et al., 2013; Van Dijk, Sabuncu, & Buckner, 2012). Therefore, several additional steps were taken in the present analysis to properly correct for motion. As a first step, we visually inspected the rigid body motion estimates for each run with the intention of discarding runs with extreme motion; however, no runs included in the gPPI analysis reached this criterion and no runs were discarded. Second, local effects of head motion typically result in large and immediate signal magnitude changes, or spikes, that are qualitatively different than the slower BOLD signal response and temporally coupled to the head movement itself (Birn, Bandettini, Cox, Jesmanowicz, & Shaker, 1998). If any one of the six rigid body motion parameters indicated that head movement exceeded 5 mm, the influence of those volumes was corrected for by using 'soft removal'. Problematic volumes were soft-removed by way of setting the predictor value for that time point in the

design matrix to zero, as opposed to the addition of a regressor into the design matrix with the predictor value of that time point set to one. This has been referred to as 'soft' removal of motion spikes (Christodoulou et al., 2013) and was preferred to a hard removal of motion spikes through spike regression due to evidence that the spike regression technique may systematically bias results, especially in populations in which head motion is generally high, because it results in the removal of a substantial amount of data, thereby decreasing the degrees of freedom for some subjects relative to others (Yan, Craddock, He, & Milham, 2013; Yan et al., 2013). Of the 1674 volumes used for gPPI analysis, only 8 volumes were corrected, with no more than 2 volumes corrected in any particular run and with volume corrections occurring in different conditions for each of the 4 subjects affected. Finally, the rigid body transformation parameters were included in the gPPI design matrix as predictors of no interest (Bullmore et al., 1999; Weissenbacher et al., 2009).

Inclusion of the rigid body motion parameters is an effective way of regressing out variance due to head motion and it is often accompanied by the inclusion of second- and third-derivatives to account for the temporally delayed magnetic susceptibility effects from the head motion (Friston, Williams, Howard, Frackowiak, & Turner, 1996; Johnstone et al., 2006; Power et al., 2012; Van Dijk et al., 2012). However, because gPPI models already suffer from problems of co-linearity due to the high number of predictors (McLaren et al., 2012), we opted to not include second- or third-order derivatives. Additional motion analyses were conducted to evaluate the possible influence of head motion on our results. The results of thes analysis are reported in Appendix A.

Seed selection for gPPI analysis. Because our primary interest was to assess functional connectivity among visual and motor regions during letter processing, we functionally localized peak regions in each individual that responded more to letters than to a rest condition. This contrast, ((dLet+trLet+tyLet)>3fixation) at $p_{vox} < 0.05$, uncorrected (Table 1; Figure 2) resulted in activation in an anterior location within the L FuG and R FuG in 11 of the 15 participants, resulting in a total of 29 runs used in the present analyses. Runs used to functionally localize seeds were discarded from further

Table 1.
Specifications of Individual Subject Seed Regions.

Seed	Subject	Cluster Size (voxels)	Center (x, y, z)	Mn x	Mx x	Mn y	Mx y	Mn z	Mx z
L FuG	AB	596	(-36,-65,-13)	-41	-32	-68	-60	-18	-9
	BD	573	(-35,-41,-13)	-40	-31	-46	-37	-17	-9
	DS	220	(-26,-40,-12)	-30	-23	-44	-37	-15	-8
	EB	433	(-31,-55,-4)	-37	-28	-59	-51	-9	0
	HM	256	(-38,-44,-17)	-43	-34	-47	-38	-22	-14
	KJ	402	(-39,-42,-17)	-43	-34	-47	-38	-21	-12
	MM	139	(-42,-32,-17)	-46	-37	-33	-29	-19	-13
	PM	382	(-38,-31,-18)	-43	-34	-36	-28	-22	-15
	SS	145	(-45,-47,-9)	-49	-41	-50	-43	-11	-6
	TB	659	(-35,-55,-11)	-40	-31	-60	-51	-14	-6
	TM	849	(-34,-43,-11)	-39	-30	-48	-39	-16	-7
R FuG	AB	246	(30,-40,-6)	26	35	-43	-34	-12	-3
	BD	591	(32,-38,-11)	26	35	-43	-34	-15	-6
	DS	211	(27,-35,-18)	24	32	-39	-32	-20	-15
	EB	319	(26,-57,-9)	22	31	-59	-50	-12	-6
	HM	733	(36,-37,-15)	32	40	-41	-32	-19	-10
	KJ	655	(33,-41,-17)	28	37	-45	-36	-22	-13
	MM	105	(31,-39,-16)	26	32	-43	-34	-20	-12
	PM	382	(26,-45,-15)	21	30	-49	-40	-18	-11
	SS	341	(41,-40,-8)	37	45	-44	-35	-11	-6
	TB	946	(26,-50,-8)	22	31	-55	-46	-13	-4
	TM	761	(33,-38,-12)	29	38	-43	-34	-17	-8

All selected seed regions were significant at $p_{vox} < 0.05$, uncorrected. L FuG: left fusiform gyrus. R FuG: right fusiform gyrus. Mn: Minimum. Mx: Maximum.

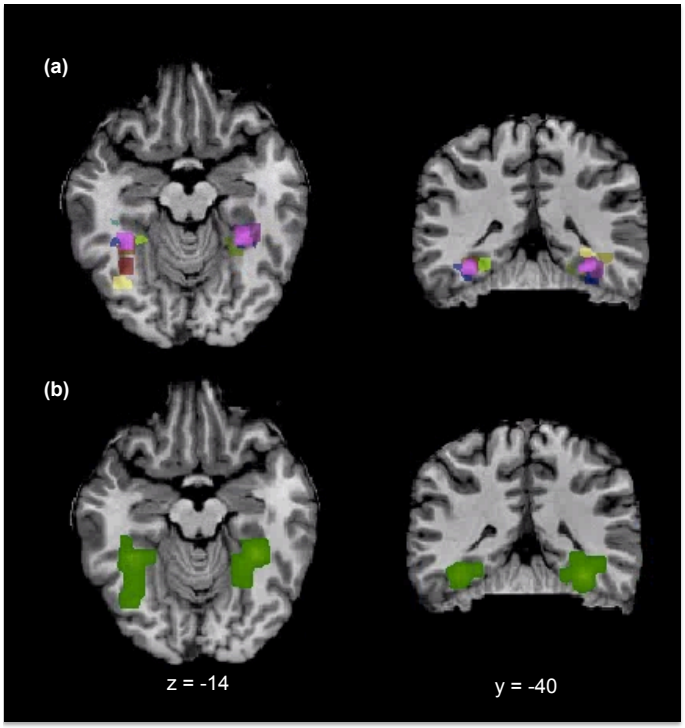

Figure 2. Localization of Individual Seed Regions for gPPI Analysis. (a) Individual seeds localized to the left and right fusiform gyri by contrasting all trained letter conditions to a fixation baseline. Each subject is represented by a different color. **(b)** Probability map showing the spatial consistency of the seed regions across individual subjects on a template brain.

analyses, leaving 18 runs for gPPI analysis. Discarding runs used to localize seeds may not have been necessary; however, we know of no published research demonstrating that reusing these runs is an acceptable practice for gPPI analyses. Therefore, we elected to err on the side of caution, and ran the gPPI analysis using only the runs that were not used to localize the seed regions.

gPPI analysis. Separate gPPI analyses were performed for each seed region and within each individual. Time courses were extracted from each individual seed region and were demeaned, creating unique physiological predictors for the L FuG and R FuG seeds for each individual run. The gPPI predictors were created through an element-wise multiplication between each psychological predictor, one for each task, and a particular physiological predictor, creating unique gPPI predictors for each individual run. Performing gPPI at the individual level resulted in subject-specific voxel-wise beta-weights that corresponded to the strength of the correlation between the signal from that voxel and each of the unique psychological, physiological, and interaction predictors.

We then performed a series of whole brain contrasts at the group level targeted at determining differential functional connections associated with visual-motor training with letters. First, to test for effects of training overall, trained stimuli were compared to untrained stimuli. Second, to assess the effects of stimulus type within training, all trained letter conditions were contrasted against all trained shape conditions. Third, we performed contrasts to characterize the effects of the different training conditions within letters by contrasting each condition to untrained letters. We followed this contrast with a conjunction analysis to determine the degree to which the different training conditions influenced the same functional connections. Fourth, to assess the potential of stimulus-specific from self-production (handwriting and drawing) we compared letters trained through handwriting to shapes trained through drawing. Finally, to contrast the different types of visual-motor learning within letters, we compared the training conditions to one another. Resulting statistical maps were subjected to cluster thresholding at the $p_{voxel} < 0.05$, $p_{cluster} < 0.05$ significance levels through Monte Carlo simulations iterated 1000 times (Forman et al., 1995). Cluster corrected maps were used as component maps in the conjunction analysis.

Table 2.
Specifications of Regions Functionally Connected to the L FuG and R FuG by Contrast.

Seed	Contrast	Cluster Size (voxels)	Pk T	Pk (x,y,z)	Mn x	Mx x	Mn y	Mx y	Mn z	Mx z
L FuG	(dLet+dSh+trLet+ trSh+tyLet+tySh) >3(cLet+cSh)	10988	3.38	(32, -41, 15)	-10	65	-54	-25	1	67
	(dLet+trLet+tyLet) >3cLet	15226	4.24	(-43,-75,-23)	-56	11	-88	-40	-40	-17
		3985	3.59	(32,-38,9)	13	37	-44	-20	-12	30
		8647	3.37	(41,-35,36)	23	69	-50	-22	13	58
	((dLet+trLet+tyLet) >(dSh+trSh+tySh)) >(3(cLet>cSh))	7529	3.58	(-43,-74,-24)	-53	17	-87	-55	-40	-15
	dLet>cLet	6717	5.81	(17,-23,42)	-35	20	-47	-5	15	47
		6104	4.44	(66,-29,30)	23	66	-59	-19	24	51
	(dLet>cLet) >(dSh>cSh)	--	--	--	--	--	--	--	--	--
	trLet>cLet	3756	5.00	(47, 29,39)	39	66	-37	-17	23	49
	(trLet>cLet) >(trSh>cSh)	6828	4.05	(47,-23,51)	32	66	-44	-17	21	57
	tyLet>cLet	5144	4.86	(47, 44,51)	29	66	-66	-27	29	57
	(tyLet>cLet) >(tySh>cSh)	2906	4.21	(59,-35,35)	40	66	-42	-22	29	52
	dLet>dSh	4797	5.31	(-52,16,9)	-59	-31	4	27	30	-3
	dLet>trLet	--	--	--	--	--	--	--	--	--
	dLet>tyLet	4206	4.36	(-13,-35,48)	-41	-7	-51	-14	29	67
	trLet>tyLet	--	--	--	--	--	--	--	--	--
	(dLet>tyLet) >(dSh>tySh)	--	--	--	--	--	--	--	--	--
	(dLet>cLet)& (trLet>cLet)& (tyLet>cLet)	902	--	--	39	66	-36	-24	25	48

R FuG	(dLet+dSh+trLet+trSh+tyLet+tySh)>3(cLet+cSh)	--	--	--	--	--	--	--	--	--
	(dLet+trLet+tyLet)>3cLet	--	--	--	--	--	--	--	--	--
	((dLet+trLet+tyLet)>(dSh+trSh+tySh))>(3(cLet>cSh))	--	--	--	--	--	--	--	--	--
	dLet>cLet	--	--	--	--	--	--	--	--	--
	(dLet>cLet)>(dSh>cSh)	--	--	--	--	--	--	--	--	--
	trLet>cLet	2791	3.92	(32, -47, 48)	13	63	-56	-26	36	57
	(trLet>cLet)>(trSh>cSh)	--	--	--	--	--	--	--	--	--
	tyLet>cLet	--	--	--	--	--	--	--	--	--
	(tyLet>cLet)>(tySh>cSh)	--	--	--	--	--	--	--	--	--
	dLet>dSh	--	--	--	--	--	--	--	--	--
	dLet>trLet	--								
	dLet>tyLet	--	--	--	--	--	--	--	--	--
	trLet>tyLet	--								
	(dLet>tyLet)>(dSh>tySh)	--	--	--	--	--	--	--	--	--

All results are reported at $p_{vox} < 0.05$, $p_{cluster} < 0.05$. L FuG: left fusiform gyrus. R FuG: right fusiform gyrus. Pk: peak. Mn: Minimum. Mx: Maximum.

Results

Functional Connectivity Analysis

Effects of training (trained vs. untrained stimuli). (Figure 3) To ensure that our training had an effect and to quantify that effect, we compared all trained symbols, including letters and shapes, to symbols with which they received no training, (dLet+dSh+trLet+trSh+tyLet+tySh)>(3(cLet+cSh)). Significant functional connectivity between the L FuG and right hemisphere superior parietal lobule (SPL), inferior parietal lobule (IPL), inferior parietal sulcus (IPS) and the posterior cingulate cortex (PCC) was observed to be greater for trained vs. untrained stimuli. There were no areas of greater functional connectivity for this contrast with the R FuG. A widespread right parietal system was, therefore, functionally connected with the L FuG during perception as a result of training, indicating that functional connections may occur after relatively brief training experiences.

Stimulus-specific training (trained letters vs. trained shapes). To assess the effects of training that may have been specific to letter stimuli, we compared connectivity patterns that resulted from comparing trained vs. untrained letters to trained vs. untrained shapes (((dLet+trLet+tyLet)>(dSh+trSh+tySh))>(3(cLet>cSh))). This analysis showed no difference in connectivity with the seed regions for trained letters vs. trained shapes, indicating that the training effect seen in our first analysis was not specific to letters.

Training effects within letters (each trained letter condition vs. untrained letters). (Figure 4) To better understand the training effects within letters, we then focused on the type of visual-motor training by comparing each of the three methods of visual-motor training to *untrained* letters. Contrasting letters trained through handwriting to untrained letters (dLet > cLet), letters trained through tracing to untrained letters (trLet > cLet), and letters trained through typing to untrained letters (tyLet > cLet), all revealed an increase in functional connections between the L FuG seed and R IPS/SPL with the cluster being nearly exactly the same for each contrast (Figure 4a). No areas were more functionally connected with the R FuG seed for letters trained through handwriting or through typing compared to untrained letters; however, contrasting letters trained through tracing to untrained letters revealed an increase in

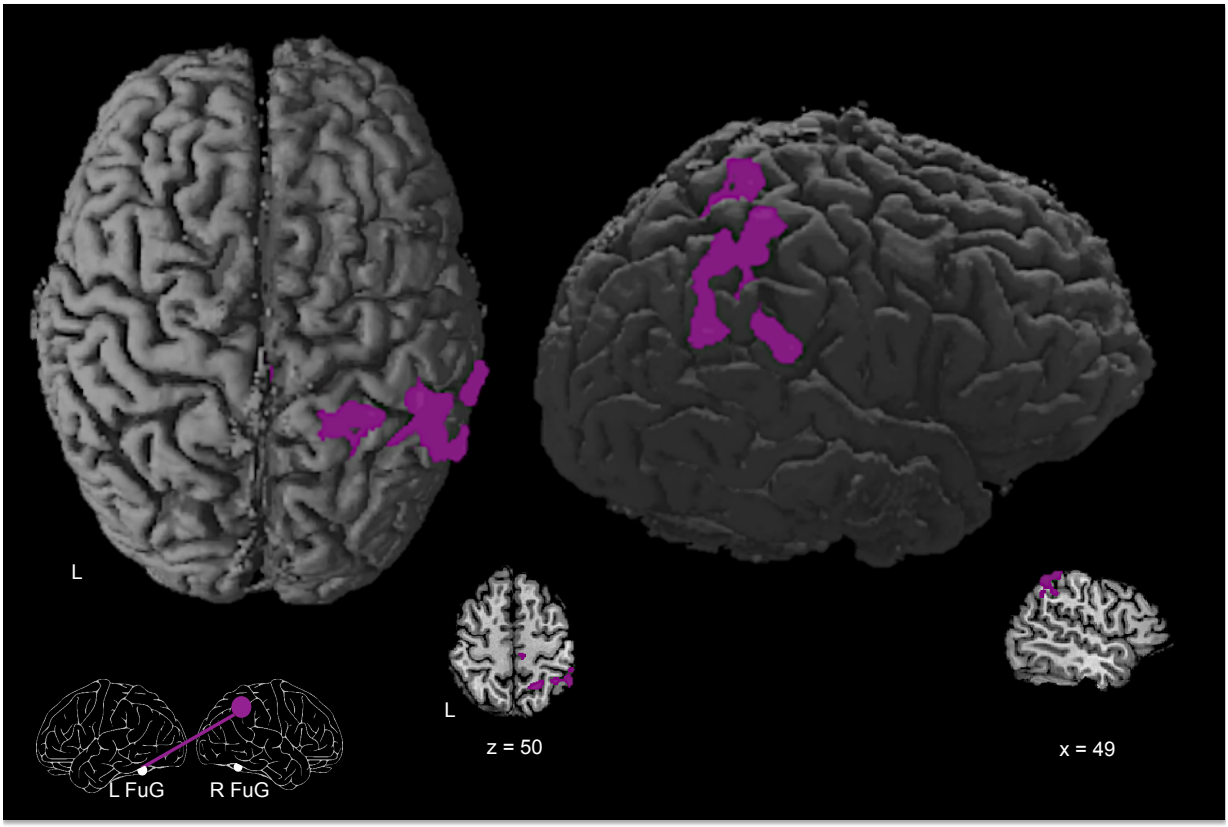

Figure 3. Effects of Sensorimotor Training with Symbols. Functional connections between the L FuG and a right parietal region (purple), including the R SPL, R IPS, and R IPL, for the perception of trained letters and shapes compared to untrained letters and shapes. Talairach coordinates are provided. Sagittal view is of the right hemisphere.

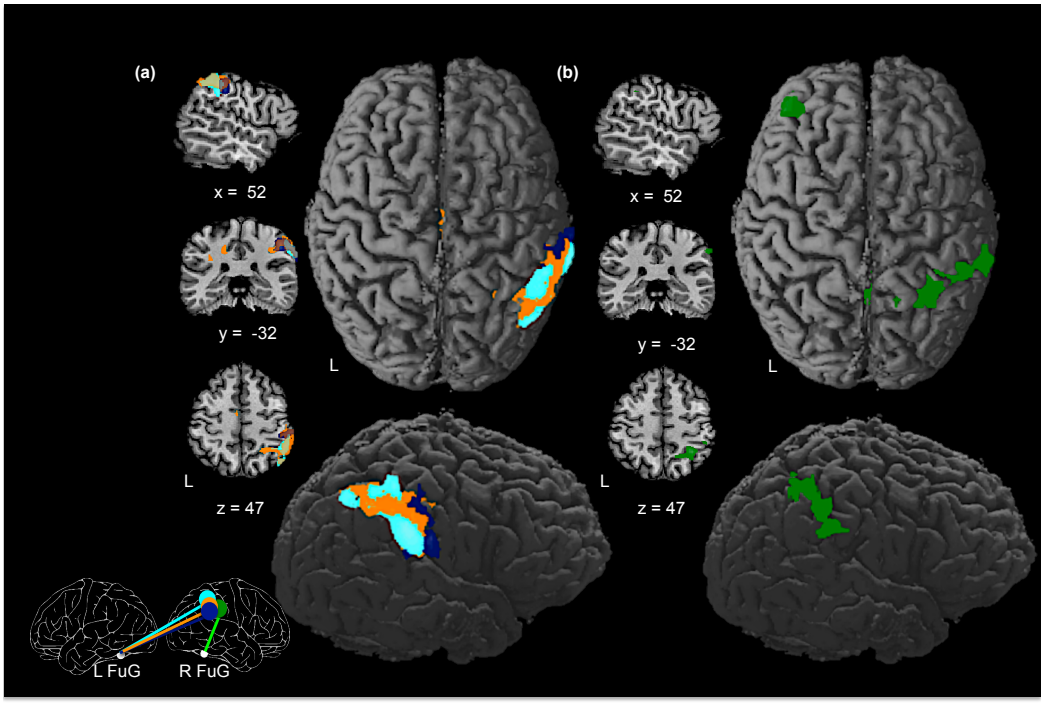

Figure 4. Effects of Sensorimotor Training with Letters. (a) Functional connections between the L FuG and a right parietal region, including the R SPL, R IPS, and R IPL, for the perception of letters trained through handwriting (orange), tracing (dark blue), and typing (cyan) compared to untrained letters. (b) Functional connections between the R FuG and a right parietal region and L MFG for the perception of letters trained through tracing (green) compared to untrained letters. Talairach coordinates are provided. Sagittal view is of the right hemisphere.

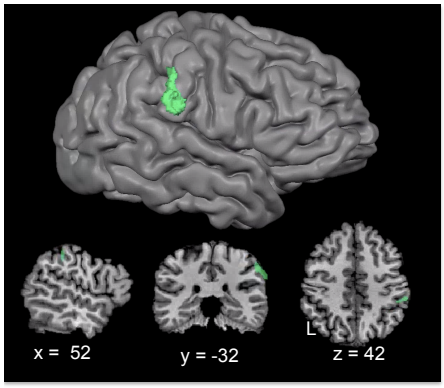

Figure 5. Conjunction Analysis of Contrasts Presented in Figure 4a. Functional connections between the L FuG and anterior R IPS/IPL (turquoise) were stronger during the perception of letters trained through drawing and letters trained through tracing and letters trained through typing than untrained letters. Talairach coordinates are provided. Sagittal view is of the right hemisphere.

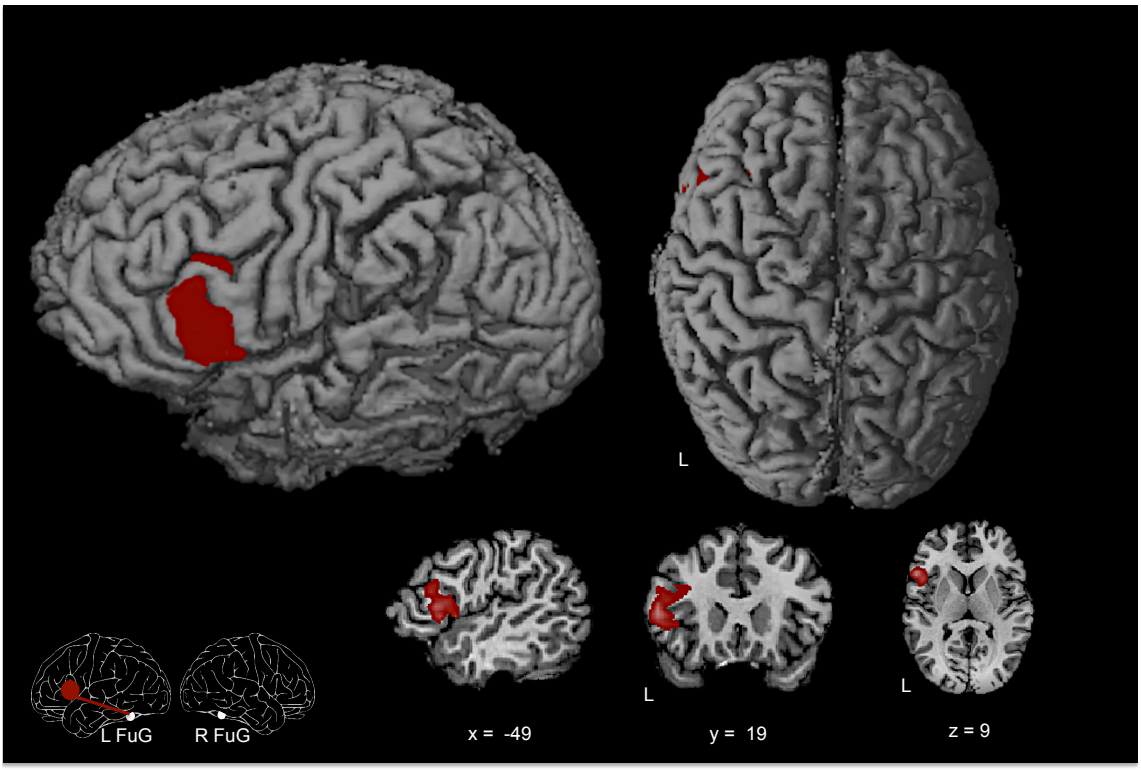

Figure 6. Effects of Handwriting Experience as a Function of Stimulus Type. Functional connections between the L FuG and L IFG (cayenne) for the perception of letters trained through handwriting compared to shapes trained through drawing. Talairach coordinates are provided. Sagittal view is of the right hemisphere.

functional connections between the R FuG seed and R IPS/SPL and L MFG (Figure 4b).

We investigated these results further by performing a conjunction analysis on the cluster corrected statistical maps produced by comparing functional connections with the L FuG during the perception of letters trained through handwriting, letters trained through tracing, and letters trained through typing to untrained letters. This analysis revealed that drawing letters, tracing letters, and typing letters all contributed to an increase in functional connections between the L FuG and a relatively restricted region of the anterior R IPS/IPL (Figure 5).

Stimulus-specificity for handwritten production (handwriting letters vs. drawing shapes). (Figure 6) To compare the effects of self-production as a function of stimulus type, we directly compared the effects of handwriting letters to drawing shapes (dLet>dSh). This contrast revealed greater functional connectivity between the L FuG seed and a left premotor area, the L IFG, for letters trained through handwritting than shapes. No areas were functionally connected with the R FuG for this contrast.

Effects of the type of visual-motor training with letters: handwriting vs. tracing and typing. (Figure 7) Our fifth hypothesis was that positive effects in visual-motor functional connectivity from handwriting practice with letters would display some specificity to the visual-motor training method. To test this hypothesis, we compared the three conditions of visual-motor training to one another within letters. First, we compared letters trained through handwriting to letters trained through tracing (dLet>trLet). Then, we compared letters trained through tracing to letters trained through typing (trLet>tyLet). Finding that no areas were more functionally connected with either the L FuG or the R FuG for either contrast, we then compared letters trained through handwriting to letters trained through typing (dLet>tyLet). This contrast revealed an increase in functional connections for letters trained through handwriting between the L FuG seed and a left dorsal sensorimotor area, encompassing L dPrG, L dPoG, and the area of the central sulcus between them. No areas were more functionally connected with the R FuG seed for these contrasts. No significant functional connections remained after controlling this contrast for drawing practice with shapes ((dLet>tyLet)> (dSh>tySh)) for either the L FuG or R FuG seeds, however. The effects seen above for the comparison of handwriting vs. typing may not be specific

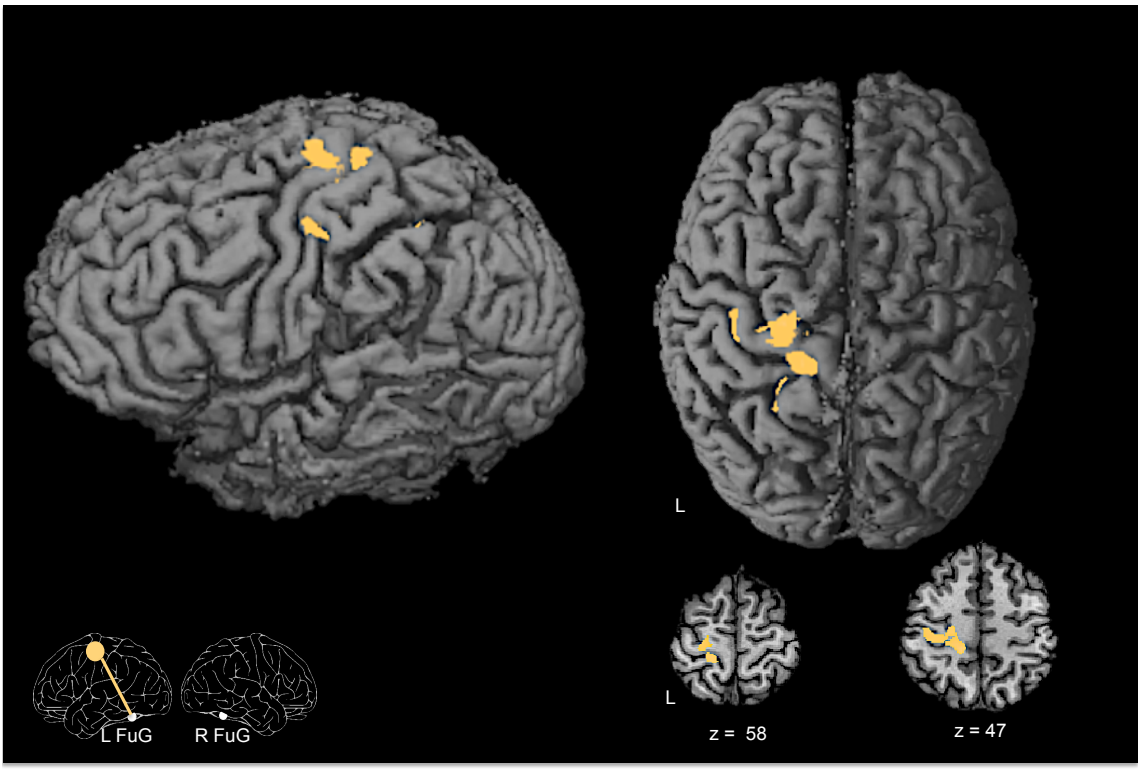

Figure 7. Effects of Handwriting vs. Typing Experience with Letters. Functional connections between the L FuG and dorsal sensorimotor area (yellow), including the L dPrG and the L dPoG, for the perception of letters trained through handwriting compared to letters trained through typing. Talairach coordinates are provided.

to letters; rather, they appear to be most associated with handwriting experience.

Discussion

Previous research has shown that letter production increases activation in both ventral-temporal and motor brain regions during passive perception in preliterate children (James, 2010; James & Englhardt, 2012) and in literate adults learning novel pseudoletters (James & Atwood, 2009). Our results suggest that the engagement of these visual and motor regions during letter perception can be attributed, at least in part, to the emergence of a visual-motor functional network during letter perception. The presence of visual-motor functional connectivity suggests that the functioning of visual and motor brain regions during letter perception was not completely independent of one another but, rather, that there was a certain degree of information transferred among them.

In the following, we first consider the broad visual-motor network that results from visual-motor training in general and then, more specifically, we consider how different types of training with letters affected functional connectivity patterns. We then discuss results that suggest that components of this network have different functions for supporting visual letter processing. Namely, functional connections between the visual and parietal regions appear to be related to visual-motor training in general, connectivity between visual regions and ventral frontal regions increased as a result of writing letters compared to shapes, and functional connections between visual and dorsal frontal regions increased as a result of handwriting letters compared to other visual-motor training methods.

Fusiform Gyri – Right Parietal Cortex: Training

The functional connectivity found between the L FuG and the R parietal cortex, specifically the R SPL, R IPS, and R IPL, was revealed in a variety of contrasts that targeted the effects of training. Our overall training contrast, comparing the perception of trained symbols vs. untrained symbols, resulted in functional connectivity between the L FuG visual region and right parietal cortex, as did our contrasts between the specific training conditions with letters and untrained letters. This right parietal region also displayed functional connections with the R FuG for the perception of letters learned through tracing vs. untrained letters, which was the only contrast showing significant functional connections with the R FuG.

Furthermore, a conjunction analysis confirmed that handwriting, tracing, and typing training all increased functional connections between the L FuG and an anterior portion of the R IPS/IPL during subsequent letter perception. We, therefore, regard this pathway as reflecting visual-motor training, in general.

One interpretation is that this pathway is involved in the visual to motor transformation required to accomplish all writing, tracing, and typing tasks. Communication between visual and motor brain regions may use transformations accomplished through parietal cortex to effectively communicate between visual and motor brain regions. Such an interpretation would appear to receive support from the breadth of studies demonstrating the involvement of parietal cortex in visually guided actions (Milner & Goodale, 2006). However, the typical finding has been that activation in *left* parietal cortex is stronger during the perception of letters learned through handwriting (James & Engelhardt, 2012) and during the act of handwriting itself. For instance, a recent study from Kadmon Harpaz et al. (2014) found that the *left* IPS was routinely recruited while participants wrote individual letters and that the pattern of activation within this region was specific to the letter being written (e.g., e vs. a). On the other hand, there are indications that both left and right parietal cortex are recruited while writing individual letters, although activation in left parietal cortex is generally stronger than in right parietal (Longcamp et al., 2014). Nonetheless, finding functional connections between the fusiform gyri and *right* parietal cortex was unexpected. We can only attribute this difference to the fact that prior studies did not look at functional connectivity. Rather, they looked at changes in the height of activation across tasks. Given that this is an unexpected result and the absence of prior studies looking at functional connections during letter perception and handwriting, this result is particularly difficult to interpret.

Perhaps the most parsimonious interpretation is one that involves attention and effort when perceiving newly learned forms. The right parietal lobe has been considered for many years to be important for visual attention (Vandenberghe, Molenberghs, & Gillebert, 2012). Our findings would fit well with such an interpretation if we assume that processing recently learned stimuli recruits more attentional mechanisms than processing well-learned stimuli. Similarly, recent visual-motor experiences may make certain spatial features of the letterforms more salient and, thus, the fusiform and right parietal

functional connections may be due to the orienting of spatial attention for the purpose of letter recognition. Such an interpretation would be supported by studies that have indicated a role for R IPS in the visual perception of newly learned forms (Milner & Goodale, 2006). Without directly manipulating attention in the current study, however, such interpretations should be considered with caution.

Fusiform Gyri – lnferior Frontal Gyrus: Written Language Pathway

The pathway between the left visual cortex and the L IFG has long been thought to underlie language processing. Numerous studies, dating back to Broca (Broca, 1861), have suggested a crucial role for the L IFG in language production. The L IFG has traditionally been associated with speech articulation; however, handwriting, being one form of language production, also recruits this region (James & Gauthier, 2006). Here, we find that this region is functionally connected to the L FuG – a language region associated with the visual perception of orthography in the left visual cortex – during the perception of letters learned through handwriting when compared to shapes learned through drawing.

If we consider the L IFG as playing a crucial role in the sequencing of motor actions – whether in speech articulation or handwriting – we might consider that the L FuG – L IFG connection may be strengthened by sequential actions. For instance, practice reproducing written forms that require a specific motor sequence would increase the utility of this region during subsequent visual perception of the practiced form. A similar mechanism may be at work in phonological processing. Practice articulating a letter sound requires a specific motor sequence that may increase the utility of this region during subsequent auditory perception of the practiced sound. If the L IFG is concerned with the ordering of motor movements to produce speech and written symbols, then experiences that direct the attention of the observer to the relationship between the motor sequence and the features produced, auditory or visual, may effectively train this area to more readily realize the relationship between important features for the purpose of perception. The role of the L IFG in the sequencing of motor actions is supported by the earlier finding that the L IFG response is increased after handwriting and tracing practice with letters compared to typing (James & Engelhardt, 2012). Here, we show that the L IFG response is more highly correlated with the L FuG response during the perception of letters learned through handwriting than shapes learned

through drawing. We interpret this functional connection as a visual-motor connection that may be strengthened by the stroke-by-stroke creation of visual features through sequential motor actions.

Given that the L IFG is traditionally associated with the speech articulation, an obvious alternative interpretation of this finding is that the L FuG is being driven by the visual stimulus at the same time that the L IFG is being recruited for sub-vocal articulation and, thus, these two regions exhibit correlated activity. This is not likely for two reasons. First, the gPPI method explicitly accounts for the main activation associated with the task, and so, the functional connections observed between the L FuG and L IFG are task-based correlations that are present above and beyond any co-activation driven by independent aspects of the task (e.g., visual letter perception, sub-vocal articulation). Second, if this correlation were due to the simultaneous, yet independent, effects of visual letter perception and sub-vocal articulation, then it would be expected that the correlation strength would be greater in all letter conditions when compared to shape conditions. This was not the case, however.

Left Fusiform Gyrus – Left Precentral and Postcentral Gyri: Specificity of Handwriting Practice

Perhaps most interestingly, when we compared handwriting experience to typing experience during subsequent letter perception, a functional pathway from the left visual regions to the left dorsal primary motor/somatosensory cortices was revealed. That is, activation patterns in the L FuG were more correlated with patterns in the L dPrG/dPoG when children perceived letters with which they had received handwriting rather than typing training. Handwriting's ability to strengthen functional connections between the L FuG – L dPrG/dPoG indicates that handwriting may be particularly effective at pairing motor and proprioceptive information with visual information for the purpose of visual perception. The L dPrG is a well-documented primary motor region and the L dPoG is a well- documented somatosensory region (Chouinard & Paus, 2006; Tate, Herbet, Moritz-Gasser, Tate, & Duffau, 2014). Both regions are known to function together during motor actions and their coordination is particularly important during fine motor movements, such as handwriting (Deng et al., 2014; Sun et al., 2015). The integration of motor and somatosensory regions during writing may be more related to the necessity of using proprioceptive feedback from a writing implement to modulate fine motor movements, which is relevant during

handwriting practice, but not during typing practice. Our results indicate that the coordination of motor and somatosensory brain regions is influential in guiding perceptual decisions about visually presented stimuli with which the observer has received stimulus-specific motor training (i.e., creating a form feature-by-feature). This interpretation is in line with behavioral results from James and Gauthier (2009), in which motor execution and proprioceptive feedback elicited during handwriting interfered with visual letter recognition performance and with neuropsychological case studies indicating that one's ability to write letters is related to one's ability to visual recognize letters (Anderson et al., 1990; Bartolomeo, Bachoud-Lévi, Chokron, & Degos, 2002). In light of these studies, our results indicate a functional role for motor and somatosensory systems in visual letter recognition by way of functional communication pathways between L FuG and L dPrG/dPoG.

Conclusion

We proposed that the engagement of both visual perceptual and motor regions during letter perception was driven by the emergence of a functional network comprised of the visual and motor systems that were used during letter production. Here, we took the first step towards providing evidence in support of this proposal. We demonstrated that a visual-motor functional network was engaged during letter *perception* in preliterate children after letter production practice. To conclude that this visual-motor functional connectivity during perception was a re-engagement of the neural systems that were used during letter production, we must also provide evidence for two additional claims. First, we must demonstrate that a visual-motor functional network supports letter production. Evidence in support of this claim is presented in Chapters 3 and 4. Second, we must demonstrate that the visual-motor functional network that supports letter perception is similar to the network that supports letter production. This will be addressed in Chapter 4.

The final chapter addresses two hypotheses generated by the current experiment. First, it addresses whether or not the visual-motor contingency inherent to letter production results in functional connectivity among visual and motor brain regions during perception. The emergence of these visual-motor communication pathways appeared, for the most part, to be related to the training experience.

Functional connectivity between the L FuG and the L dPrG was greater when children were presented with letters (or shapes) trained through drawing and tracing when compared to letters (or shapes) trained through typing and was no different for letters trained through drawing compared to tracing. This particular connection was, therefore, not specific to letters and was due to a component that is shared between drawing and tracing, but not typing. The obvious similarities are that a form is created, feature by feature, through a movement pattern that is specific to the written product, and that both handwriting and tracing occur through the use of a writing implement. Our interpretation was that drawing and tracing both required a stimulus-specific motor movement using similar hand positions and similar visual guidance and, importantly, created a visual percept of the letter that was spatiotemporally contingent on the motor movements used to create it. I, therefore, hypothesize that the visual-motor contingency—the real-time coupling between visual and motor experiences of a letter as it is being produced—results in visual-motor functional connectivity among visual and motor brain regions during subsequent perception.

Second, it addresses if the emergence of this visual-motor functional connectivity is related to gains in visual letter recognition. There is evidence to suggest that communication among sensory and motor systems supports literate recognition processes. Individuals who lack the ability to produce letters by hand demonstrate impaired letter recognition abilities (Anderson et al., 1990) and producing a letterform facilitates mental manipulations of letters in individuals with impaired letter imagery abilities (Bartolomeo et al., 2002). There is, furthermore, evidence that as the amount of experience with a written symbol increases, sensory and motor systems increasingly interact with each other during letter processing. James and Gauthier (2009) demonstrated that *over*learned stimuli (e.g., letters) were particularly susceptible to perceptual identification errors when observers were asked to simultaneously write a categorically different, but perceptually similar, letter, such as writing the uppercase letter G while visually perceiving the uppercase letter C. The motor action along with proprioceptive feedback while writing one letter was enough to cause errors in visual identification of a different letter when both occurred simultaneously. These results suggest that communication among sensory and motor systems contributes to literate letter perceptual processes. We, therefore, hypothesize that the emergence of visual-

motor functional connectivity during letter perception supports the gains in letter recognition that so often accompany production training (Longcamp et al., 2005; Zemlock et al., 2018).

CHAPTER 3:

AN ANALYSIS OF THE BRAIN SYSTEMS

INVOLVED WITH PRODUCING LETTERS BY HAND

This chapter focuses on characterizing the neural response during letter production to provide preliminary evidence for the claim that letter production is supported by a functional network comprised of visual and motor regions. The evidence provided in this chapter is preliminary in the sense that it does not address the presence of a functional network during letter production directly but, rather, addresses the relative participation of brain regions in the visual-perceptual, visual-motor, and motor components of letter production. It is important to establish the relative participation of brain regions in the visual and motor components of letter production so that if a functional network is observed during letter production, we will be better able to claim that this network is, indeed, a functional network comprised of visual and motor brain regions. The goal of this chapter is, therefore, to demonstrate that activation during letter production is coarsely separable into neural responses that are associated with the visual experiences of letter production and neural responses that are associated with the motor experiences of letter production.

Studies that have investigated the neural systems supporting letter production have repeatedly demonstrated that letter production is supported by a distributed frontal, parietal, and ventral-temporal neural system (James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; Longcamp et al., 2008, 2011, 2014; Planton et al., 2013; Siebner et al., 2001; Seitz et al., 1997; Yuan & Brown, 2014). Large bodies of work have documented the recruitment of motor regions in frontal cortex for action execution (for review: Schieber, 2001; Graziano, 2006; Meier et al., 2008). Activity in parietal cortex has traditionally been associated with visual-motor transformations (Jackson & Husain, 2006; Ogawa & Inui, 2009; for review Buneo & Andersen, 2006) and visually guided action (Goodale & Milner, 2005; Milner & Goodale, 2006) with anterior portions of the intraparietal sulcus (IPS) being more associated with motor movement and the posterior portions being more associated with visual feedback during movement (Haar et al., 2015; Kadmon Harpaz et al., 2014; Thaler & Gooodale, 2011; Yuan & Brown, 2014; although see Wang et al., 2017). Activity in ventral-temporal cortex has traditionally been

associated with visual object perception for the purposes of categorization (for review Grill-Spector & Weiner, 2014; although see Peleen & Downing, 2017) with several works focusing on ventral-temporal responses to the object category of letters (e.g., Cohen et al., 2000; James et al., 2005; Dehaene et al., 2001, 2002, 2004; Dufor & Rapp, 2013; Polk & Farah, 2002; Rothlein & Rapp, 2014). There is, therefore, a large amount of evidence to suggest that the frontal, parietal, and ventral-temporal responses observed during letter production may be differentially involved in motor, visual-motor, and visual perception processes.

We propose that the frontal, parietal, and ventral-temporal cortices that comprise the widespread neural system for letter production are recruited to varying degrees for the visual, motor, and visual-motor components of letter production. We, therefore, decomposed the complex act of letter production by manipulating motor production and visual feedback such that we could isolate these behavioral components. We asked fourteen literate college-aged adults to write letters with ink (motor, visual), write letters without ink (motor, no visual), and perceive dynamic re-presentations of their own handwritten letters (no motor, visual) using an fMRI-compatible writing tablet during fMRI scanning. We predicted that frontal motor regions would be most associated with motor production and that ventral-temporal cortex would be most associated with the visual perception of the forms produced. We also predicted a strong role for the parietal cortex in these productions. We predicted that the posterior parietal cortex would respond to both motor and visual components of the letter production process, due to its role in visually guided action, but would show a graded visual-motor, anterior-posterior response pattern.

Letter production involves several visual perceptual components. We, therefore, endeavored to determine the neural responses associated with each type of visual percept. During letter production, the observer presents themselves with a dynamically unfolding handwritten letter, stroke by stroke, as they are producing the letter. At the completion of letter production, they perceive their own handwritten letter. To better understand the brain systems involved with the visual perceptual components of letter production, we compared activation found during the perception of one's own letters dynamically unfolding (i.e., a video recording) to the static presentation of the final product of the letter production to

highlight responses associated with the dynamic unfolding component. We also compared the perception of their final handwritten letter product to the perception of a typed letter to highlight responses associated with the perception of handwritten letters.

Materials and Methods

Participants

Fourteen literate English-speaking adults were recruited by word-of-mouth (8 female, mean age = 20.1 years, S.D = 2.5). All participants were right-handed, as indicated by the Edinburgh Handedness Inventory (Oldfield, 1971), screened for neurological trauma, developmental disorders, and MRI contraindications. All participants provided written informed consent according to the guidelines of the Indiana University Institutional Review Board.

Materials

Stimuli. A set of 12 single upper-case letters of the Roman alphabet were selected based on the distinctiveness of their visual forms and their letter names: A, B, C, D, G, H, J, L, Q, R, U, and Y. All letters were presented/produced in white on a black background, one at a time. Typed letters were presented in 120-point Arial font and subtended 4 by 4 degrees of visual angle. All handwritten letters were written within a box that subtended 10 by 10 degrees of visual angle with a pen width of 7 points. The size and form of the letter stimuli within this box differed with and across conditions given the self-produced nature of the written stimuli.

There were two conditions that involved motor production: Write With Ink and Write Without Ink. During the “Write With Ink” condition, participants wrote a letter of the Roman alphabet on a digitizing tablet that was shown to them in real time in a mirror above the head coil. Writing trajectories and final handwritten letters from the Write With Ink condition were saved so that they could be re-presented in additional conditions (see below). During the “Write Without Ink” condition, the screen remained blank as they produced their letter, just as if their pen had no ink. Therefore, the motor production in both cases was kept relatively constant, while the resultant visual percept of the letter was either present or absent.

There were three conditions that involved passive visual perception: Watch Dynamic, Watch Static, and Watch Typed. During Watch Dynamic, participants saw a playback of their own letter production from the "Write with Ink" condition (above). The timing of the playback was the same as their own production time. During the Watch Static condition, participants saw their own handwritten letters statically presented. During Watch Typed, participants saw typed letters. The six letters used for the Write With Ink, Watch Static, and Watch Dynamic blocks were necessarily the same set of six letters. For this reason, the same six letters were also displayed in the Watch Typed condition.

Regardless of condition, the block instructions and letter-name prompts were pre-recorded from a female native English speaker and played at the beginning of each block and trial, respectively.

Apparatus. All participants completed fMRI tasks on an MR-safe tablet that records handwriting trajectories and can be used to project participants' handwritten letters onto a mirror above their head—in real time as they are producing each form (Tam, Churchill, Strother, & Graham, 2011). This handwriting-recording device has been used in several studies (e.g., Kadmon Harpaz et al., 2014, Longcamp et al., 2014).

The tablet was supported by a lap-desk that kept it in a fixed position above their lap and within arm's reach (Figure 8). Participants held an MR-safe stylus throughout the entire session and wore a Wheaton® elastic shoulder immobilizer to restrict movement necessary for writing to elbow, wrist, and hand joints.

Auditory instructions and letter-name prompts were presented through MR-safe headphones and Boom™ was used to enhance audio clarity. A Mitsubishi XL30 projector displayed all visual presentations onto a mirror in the bore of the scanner attached to the head coil above the head of the participant (Figure 8). An in-house Matlab program using the Psychophysics Toolbox extensions interfaced with the tablet, headphones, and projector to record and present all stimuli (Brainard, 1997; Pelli, 1997).

Figure 8. Full Apparatus Set Up. The MR-safe writing tablet (Tam et al., 2011), arm pillow, and Wheaton® elastic shoulder immobilizer were adjusted for each participant. Subject-specific adjustments ensured that the participants were in a comfortable writing position. Before the experiment began, an experimenter positioned their hand in an appropriate position so that they could feel where their wrist laid on the apparatus. Care was taken to instruct the participants to keep their hand toward the center of the screen.

Procedure. Prior to scanning, participants watched a video that demonstrated the tasks they would be asked to perform in the scanner. The video explained that they would be asked to 'draw' (i.e., write) and 'watch' and that sometimes they would not be able to see what they were writing. After ensuring that the participants understood their task, they proceeded to the imaging environment where they first underwent a high-resolution anatomical scan followed by 4 fMRI experimental runs. During the fMRI runs, participants wrote letters with and without ink, perceived dynamic and static re-presentations of their own written letters, and perceived typeface letters in a blocked design (Figure 9). This resulted in 5 experimental conditions: Write With Ink, Write Without Ink, Watch Dynamic, Watch Static, and Watch Typed. The experimental design originally included two additional conditions that were not of primary interest for this particular study.

Each run contained one block of each condition. At the beginning of each run, 6 letters were selected randomly without replacement from the full stimulus set of 12 letters with the additional restriction that a particular selection may not contain highly confusable letter names, such as "b" and "g" (Conrad, 1964; Hull, 1973). Block orders were pseudo-randomized, as opposed to fully randomized, to ensure that the Write With Ink condition occurred before Watch Static and Watch Dynamic conditions in each run. Given that each condition presented the same 6 letters, but in a different format, it was imperative to ensure that block order was randomized to prevent possible repetition suppression effects affecting one condition more than another. Because we averaged activation across all runs, we are confident that if repetition suppression did occur, it would not be more pronounced in one condition over another.

Scanning parameters. Neuroimaging was performed using a Siemens Magnetom TIM TRIO 3-T whole-body MRI system housed in the Indiana University Imaging Research Facility. High-resolution T1-weighted anatomical volumes were acquired using a Turbo-flash 3-D sequence: TI = 900 ms, TE = 2.67 ms, TR = 2000 ms, flip angle = 9°, with 120 sagittal slices of 1.5 mm thickness, a field of view of 192 x 192 mm, and an isometric voxel size of 1.5 mm^3. For functional images, the field of view was 192 x 192 mm, with an in-plane resolution of 64 x 64 pixels and 33 axial slices of 3.8 mm thickness per

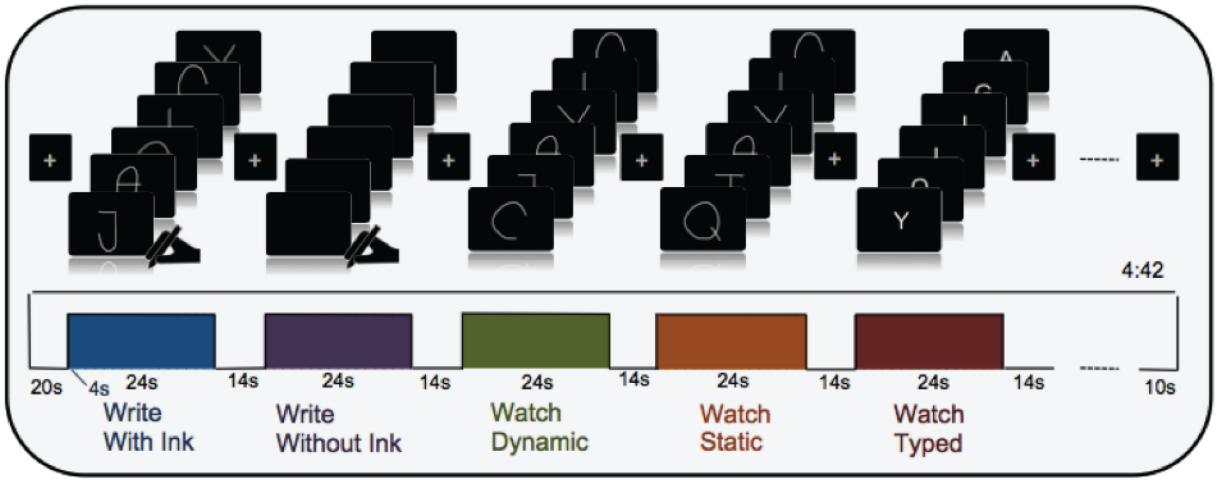

Figure 9. Stimulation Protocol. The figure presents a depiction of the blocks within each run and the trials within each block. Block orders were pseudo-randomized and counter-balanced across runs. The six letters used for the Write With Ink, Watch Static, and Watch Dynamic blocks were necessarily the same set of six letters and the same set of six letters was also displayed in the Watch Typed condition. Letter orders within a block were randomized. Block instructions and letter names were pre-recorded. Block instructions were played at the beginning of each block to alert participants to the task. Letter names were played at the beginning of each trial to alert the participant to the letter that they should write or to the letter that would be displayed.

volume with 0% slice gap, producing 3.0 x 3.0 x 3.8 mm voxels. Functional images were acquired using a gradient echo EPI sequence with interleaved slice order: TE = 30 ms, TR = 2000 ms, flip angle = 70° for blood-oxygen-level-dependent (BOLD) imaging.

Each block consisted of 6 stimuli, one presented in each of the 6 trials within a block. The order of the six letters within each block was randomized. Each trial lasted for 4 seconds to ensure that the participants had enough time to write with and without ink. There was no gap between trials, resulting in 24-second-long blocks. Each block was separated by a 14-second inter-block interval, the last two seconds of which included auditory instructions for the next block. Auditory instructions were kept to a set of two simple one-word imperatives: “draw” and “watch”. During the inter-block interval, only the fixation cross was visible in the mirror. The same fixation cross was presented for 20 seconds before the first block of each run and for 10 seconds following the last block of each run. Each run, therefore, totaled 4:42 minutes.

Analyses

The main analyses consisted of a standard preprocessing pipeline for fMRI data and additional motion correction steps, followed by a series of planned whole brain contrasts and a conjunction analysis. All but one analysis was performed in BrainVoyager QX 2.8.2. For this one analysis, an in-house Matlab routine was used to extract the phase time-course from the complex MR signal and insert it as a predictor in the BrainVoyager design matrix file (see *Preprocessing and motion correction* section).

Preprocessing and motion correction. Individual anatomical volumes were normalized to Talairach space (Talairach & Tournoux, 1988). Preprocessing of functional data included slice scan time correction, 3-D motion correction using trilinear/sinc interpolation, and 3D Gaussian spatial blurring with a full-width-at-half-maximum of 6 mm. Temporal high-pass filtering was performed using a voxel-wise GLM with predictors that included a Fourier basis set with a cut-off value of 2 sine/cosine pairs and a linear trend predictor. During normalization, functional data were re-sampled to 3 mm^3 isometric voxels. Coregistration of functional volumes to anatomical volumes was performed using a rigid body transformation.

To account for head motion, rigid body transformation parameters were included in the design matrix as predictors of no interest (Bullmore et al., 1999) along with spike regressors for each time point at which the relative root mean squared (RMS) time course exceeded 0.5 mm (Satterthwaite et al., 2013). To account for possible perturbations in the static magnetic field due to movements outside the field of view (e.g., arm movements), demeaned 'phase regressors' were included in the design matrix as predictors of no interest (Barry et al., 2010; Cheng & Li, 2010; Cheng & Puce, 2014).

Data analyses. The statistical analyses began with a voxel-wise general linear model (GLM) with one predictor of interest for each condition and seven predictors of no interest that were included for motion correction purposes only (see *Preprocessing and motion correction* section). Each predictor of interest was convolved with a double-gamma hemodynamic response function (Boynton, Engel, Glover, & Heeger, 1996). The resulting design matrix was subjected to a Random-effects GLM analysis for planned contrasts and a conjunction analysis. Resulting t-maps were subjected to a standard voxel-wise threshold of $p_{voxel} < .001$ and a cluster threshold of 40 contiguous 3-mm isometric voxels. Correspondence between anatomical locations and significant activation clusters were determined by, first, referencing the Talairach Daemon and, second, referencing the Duvernoy (1999) human brain atlas to verify. In cases where the Talairach Daemon and Duvernoy (1999) label disagreed, the Duvernoy (1999) label was selected.

Our first contrast was designed to identify the entire letter production system, as has been done in prior work (Longcamp et al., 2014). To this end, we compared letter production with fixation (Write With Ink > Fixation) to identify regions broadly associated with producing letters by hand. We followed this preliminary contrast with several whole brain contrasts designed to determine the neural sub-systems of the broader letter production system that may be more or less involved in certain behavioral components of letter production.

Two contrasts and a conjunction analysis were used to identify regions that were related to the motor, visual, and/or visual-motor components of letter production. The first contrast identified the motor component of production by comparing activation during Write With Ink to activation during Watch

Dynamic. These two conditions were identical (i.e., yoked) in terms of the *visual* information shown to the participant and served to identify the neural sub-system of letter production associated with the motor behavioral component. The second contrast identified the visual component of letter production by comparing Write With Ink to Write Without Ink. These two conditions were identical (i.e., yoked) in terms of the motor action required from the participant and served to identify the neural sub-system of letter production associated with the visual behavioral component.

A conjunction between the motor component contrast and the visual component contrast was performed to identify regions that were involved in both motor and visual components to an equal extent. Regions revealed by this conjunction analysis would demonstrate a significant difference between activation during Write With Ink and Watch Dynamic (i.e., the motor component) that is not significantly different than the difference between activation during Write With Ink and Write Without Ink (i.e., the visual component). The resulting clusters revealed by this conjunction would, therefore, be better characterized as regions associated with the visual-motor component of letter production as opposed to only the motor or visual component.

Two additional contrasts were designed to identify brain regions that were responsive to particular visual percepts produced by letter production. The first contrast identified areas associated with the unfolding of the form produced over time (Watch Dynamic > Watch Static) to assess the effects of the perception of motion information during letter production. In both of these conditions, participants were presented with their own handwritten letter—both from the same letter production episode—with the only difference being that the presentation of the letterform unfolded overtime in Watch Dynamic and was presented statically in Watch Static. The second contrast compared the effects of viewing one's own handwritten form to a typed category exemplar (Watch Static > Watch Typed) to identify regions that might be more sensitive to the perception of handwritten forms compared with typed forms.

Results

Letter Production

The comparison of producing a letter with ink to visual fixation produced a distributed neural system that included the left precentral and postcentral gyri, right precentral gyrus, bilateral posterior superior frontal gyri, bilateral parietal cortices, and bilateral occipital and ventral-temporal regions, and the cerebellum (Figure 10a; Table 3). The expanse of this contrast was expected as it served to provide a general display of brain regions involved in the letter production task and is consistent with the general response during letter production reported in Longcamp et al. (2014) using a similar apparatus and procedure. No areas were more responsive during Fixation than during letter production. The absence of auditory cortex recruitment in this contrast can be attributed to the auditory instructions received during the last two seconds of the fixation period, resulting in a cancellation of the auditory activation that would have been expected due to the auditory prompts during Write With Ink when compared to Fixation.

Motor component. The left dorsal postcentral gyrus, left intraparietal sulcus, right ventral temporal cortex, right posterior superior frontal gyrus, and bilateral cerebellar responses were associated with the motor component of the letter production task. Included in the fronto-parietal regions were dorsal and lateral aspects of the left precentral and left postcentral gyri, the right posterior middle frontal gyrus, the left superior parietal cortex, and the left anterior to middle IPS (Figure 10b). The right ventral temporal activations included a posterior portion of the right fusiform gyrus and a lateral portion of right posterior inferior temporal gyrus (Figure 10b). No areas responded more during the perception of dynamic unfolding than for producing letters with ink.

Visual component. Bilateral parietal and ventral-temporal cortices were associated with the visual component of the letter production task as well as right posterior superior frontal gyrus. The bilateral parietal regions were middle to posterior IPS (Figure 10b). The left ventral-temporal activation included a posterior portion of the inferior temporal gyri and the posterior fusiform gyrus. The right ventral-temporal response was notably broader than the left (Figure 10b). No cerebellar activation was

found for this contrast. No regions responded stronger for producing letters without ink than for producing letters with ink.

Visual-motor component. Areas of overlap among the visual and motor components of letter production were observed in right ventral-temporal cortex, including posterior inferior temporal gyrus and posterior fusiform gyrus, in left posterior IPS, and in right posterior middle frontal gyrus (Figure 11a).

Motor and visual processing in left dorsal premotor cortex. We found no activation in the left middle frontal gyrus, commonly referred to as Exner's area (Anderson et al., 1990; Exner, 1881; Longcamp et al., 2003; Planton et al., 2013), for any of our contrasts and only found a response in left superior middle frontal sulci when we compared letter production to a fixation baseline. We were interested in further exploring this result because we would have expected to see a response in left dorsal premotor cortex for the motor component of letter production. Recent work has suggested that the left dorsal premotor cortex may function as a motoric buffer that supports the serial, stroke-by-stroke creation of written forms from stored graphemic representations (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009) while also showing sensitivity to the visual perception of the unfolding stroke orders (Nakamura et al., 2012). We thought it possible that the left dorsal premotor cortex might be involved in serial visual and motor processing, resulting in no significant differences between any of our conditions except between letter production and fixation.

To provide some evidence on the use of left dorsal premotor cortex for either serial motoric and/or visual processing, we conducted two additional contrasts. In the first contrast, we compared Write Without Ink to Watch Typed with the thought that writing without ink would correspond to serial motoric processing whereas watching a static typed letter would not engage serial processing but would control for 'letters'. In the second contrast, we compared Watch Dynamic to Watch Typed. In this contrast, Watch Dynamic would engage serial visual processing whereas Watch Typed would not. We did not use Watch Static as our control condition because there is evidence that perceiving static handwritten letters evokes similar neural mechanisms as producing letters by hand (Babcock & Freyd, 1988; Freyd, 1987; Orliaguet et al., 1997).

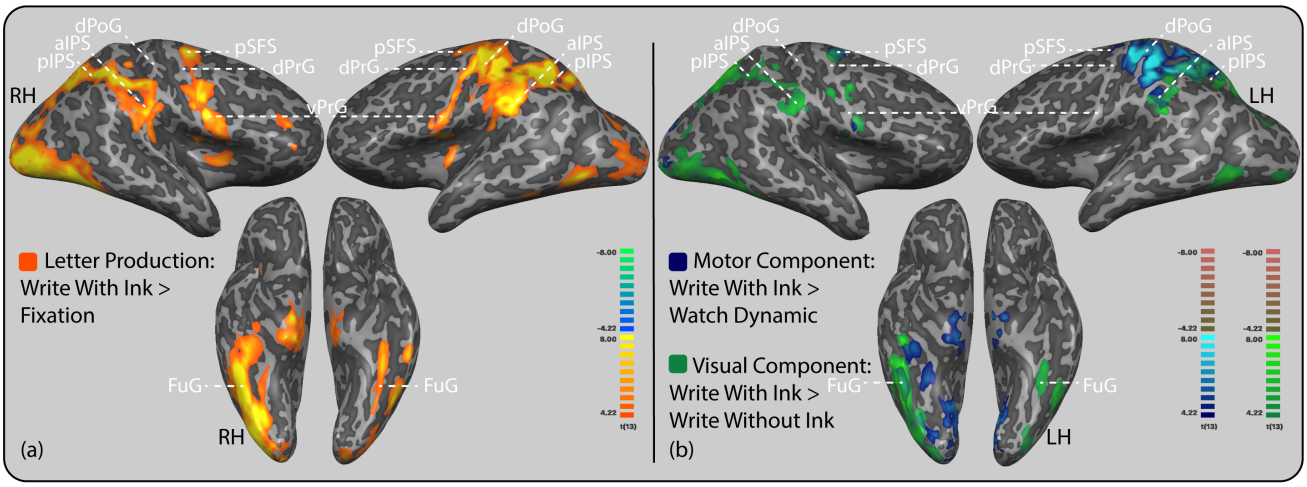

Figure 10. Motor and Visual Components of Letter Production from Whole Brain Contrasts. Letter production recruited a broad frontal motor, parietal, and ventral-temporal response, with frontal motor and anterior parietal cortices being associated with the motor component and posterior parietal and ventral-temporal cortices being associated with the visual component. (a) *Letter production system.* Areas that are orange were more active during letter production than at rest. (b) *Motor and visual neural components of letter production.* Areas that are blue were more active during letter production than watching the letter unfold (motor component) and areas that are green are more active during letter production than during letter production without ink (visual component). Group-level results are displayed at a standard voxel-wise threshold of $p_{voxel} < .001$ and a cluster threshold of 40 contiguous 3-mm isometric voxels overlaid on an inflated anatomical image from a single participant. Anatomical label abbreviations: posterior superior frontal sulcus (pSFS), dorsal precentral gyrus (dPrG), ventral precentral gyrus (vPrG), dorsal postcentral gyrus (dPoG), anterior intraparietal sulcus (aIPS), posterior intraparietal sulcus (pIPS), fusiform gyrus (FuG).

Table 3. Whole Brain Contrasts

Contrast	Nbr. of Clust.	Clust. Size (voxels)	Talairach Coordinates Peak x	Peak y	Peak z	Peak T	Anatomical Location
Write With Ink > fixation	4	118590	18	-46	-26	13.9	Right cerebellum
			-24	-58	-26	12.7	Left cerebellum
			35	-46	-14	7.5	Right post. fusiform gyrus
			29	-90	0	7.5	Right occipital lobe
			-44	-42	-23	7.0	Left post. fusiform gyrus
		49347	-33	-43	43	21.3	Left intraparietal sulcus
			-39	-22	52	11.7	Left dorsal postcentral gyrus
			-33	-19	52	10.8	Left dorsal precentral gyrus
			-36	-4	13	10.7	Left insula
			-24	-13	49	9.1	Left post. superior frontal sulcus
			-6	-7	55	8.6	Left ant. cingulate cortex
			-51	-4	37	7.1	Left ventral precentral gyrus
		31838	27	-40	40	11.8	Right intraparietal sulcus
		18495	48	2	31	9.5	Right ventral precentral gyrus
			24	-13	49	9.3	Right post. superior frontal sulcus
Motor Component: Write With Ink > Watch Dynamic	3	118665	24	-40	-26	10.3	Right cerebellum
			-24	-55	-29	8.8	Left cerebellum
			36	-55	-11	7.2	Right post. fusiform gyrus
		30254	-30	-40	46	10.3	Left intraparietal sulcus
			-33	-19	49	10.2	Left dorsal postcentral gyrus
			-1	5	46	6.3	Left ant. cingulate cortex
		2152	21	-10	55	6.9	Right post. superior frontal sulcus
Visual Component: Write With Ink > Write Without Ink	6	24288	42	-40	-17	11.4	Right post. fusiform gyrus
			33	-79	4	7.6	Right middle occipital gyrus
		17273	24	-61	52	8.8	Right intraparietal sulcus
		13946	-18	-67	46	7.6	Left intraparietal sulcus
		12885	-42	-67	-11	6.9	Left post. fusiform gyrus
		3034	42	-4	40	7.7	Right ventral precentral gyrus
		1791	30	-10	55	7.1	Right post. superior frontal sulcus
VM component: (Write With Ink>Watch Dynamic)&(Write With Ink>Write Without Ink)	3	10484	36	-58	-11	7.1	Right post. fusiform gyrus
		5452	-30	-46	46	6.3	Left post. intraparietal sulcus
		1114	27	-13	52	6.6	Right post. superior frontal sulcus
Unfolding: Watch Dynamic> Watch Static	0	--	--	--	--	--	--
Handwritten forms: Watch Static> Watch Typed	5	2002	-24	-64	52	8.4	Left post. intraparietal sulcus
		1916	45	-67	-8	12.6	Right post. fusiform gyrus
		1219	18	-67	49	6.9	Right post. intraparietal sulcus
		1025	42	44	22	6.4	Right prefrontal cortex
		711	27	-88	9	7.0	Right middle occipital gyrus

Local peaks with a T-statistic greater than 6.0 are reported for large clusters that spanned several anatomical locations. VM = visual-motor.

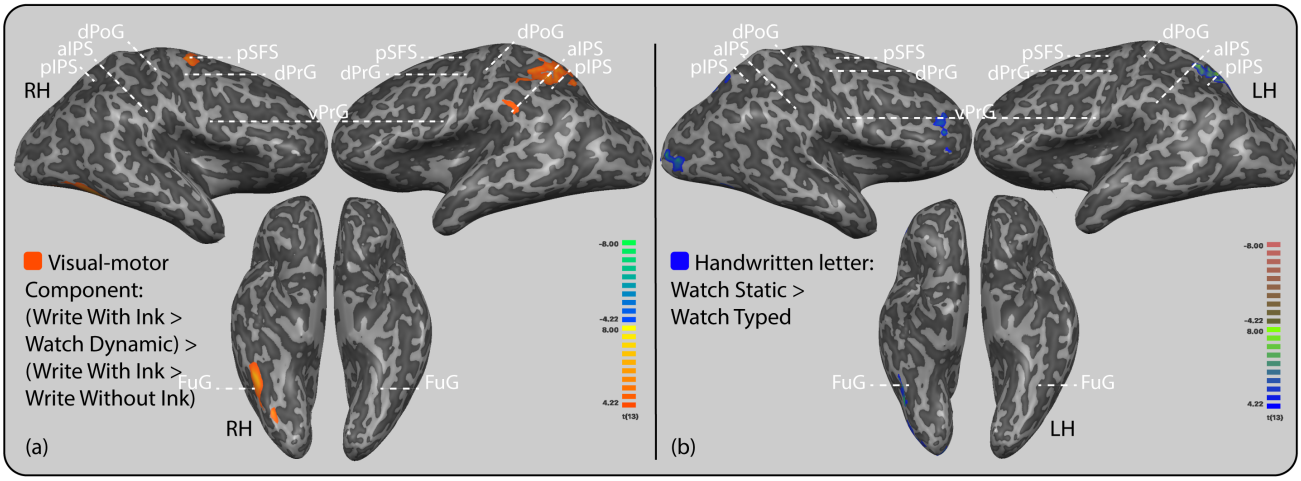

Figure 11. Conjunction of Motor and Visual Components of Letter Production and Handwritten Form Perception. A similar neural response occurred for areas involved in the visual-motor component of letter production and the perception of handwritten forms. (a) *Overlap between motor and visual components of letter production*. Areas in orange are areas that responded equally for the motor component and visual components of letter production. The results of the conjunction analysis statistically confirm overlap between motor and visual components in the bilateral posterior intraparietal sulci and in right inferior temporal gyrus. (b) *Perception of handwritten forms.* Areas that are magenta were more active while looking at a static handwritten letter than while looking at a static typed letter, these include the left posterior intraparietal sulcus, right ventral-temporal cortex, and right posterior middle frontal gyrus. Group-level results are displayed at a standard voxel-wise threshold of $p_{voxel} < .001$ and a cluster threshold of 40 contiguous 3-mm isometric voxels overlaid on an inflated anatomical image from a single participant. Anatomical label abbreviations: posterior superior frontal sulcus (pSFS), dorsal precentral gyrus (dPrG), ventral precentral gyrus (vPrG), dorsal postcentral gyrus (dPoG), anterior intraparietal sulcus (aIPS), posterior intraparietal sulcus (pIPS), fusiform gyrus (FuG).

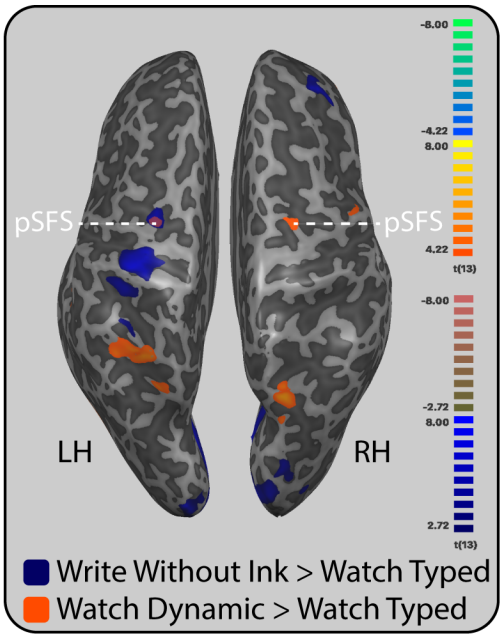

Figure 12. Motor and Visual Processing in Left Dorsal Premotor Cortex. The left superior frontal sulcus responded for serial processing in both motor and visual domains. Blue indicates regions that were more active while participants wrote letters without ink when compared to a statically presented typed letter. Orange indicates regions that were more active while participants watched a handwritten letter dynamically unfold when compared to a statically presented typed letter. Anatomical label abbreviations: posterior superior frontal sulcus (pSFS).

These analyses revealed activity in left posterior superior frontal sulcus in the left dorsal premotor cortex for both serial motoric and serial visual processing. We found responses in left posterior superior frontal sulci, left dorsal precentral gyrus, left anterior IPS/SPL, bilateral occipitotemporal cortices, and bilateral cerebellum for serial motoric processing, i.e., the comparison between Write Without Ink and Watch Typed (Figure 12). We found responses in bilateral posterior superior frontal sulci, bilateral posterior parietal cortices, and bilateral ventral temporal cortex for serial visual processing, i.e., the comparison between Watch Dynamic and Watch Typed (Figure 12).

Visual Percepts Produced by Letter Production

Unfolding. We contrasted activation levels during Watch Dynamic to Watch Static to determine areas that were related to viewing a dynamically unfolding percept. This contrast revealed no significant differences, lending support to the idea that the static handwritten percept evokes dynamic production information.

Handwritten forms. Areas that had a larger response to one's own handwritten letter than a static typed letter included bilateral posterior IPS, right occipital cortex, right posterior inferior temporal gyrus and ventral-temporal cortex, and right prefrontal cortex (Figure 11b). No areas responded more for typed letter perception than for the perception of one's own handwritten letter.

Discussion

Understanding the function of a widespread neural system requires that we understand how its components contribute to its function. In this research, we characterized the relative participation of brain regions in the motor, visual-perceptual, and visual-motor components of letter production. We determined that the letter production system involved frontal motor regions, cerebellum, ventral temporal cortex, and parietal cortex, replicating previous work (e.g., Longcamp et al., 2014), and, further, determined the relative involvement of these regions in different behavioral components of letter production (e.g., motor, visual-perceptual, visual-motor). Our results demonstrate, specifically, that frontal motor regions are most associated with motor production while ventral-temporal regions are associated with the visual perception of the forms produced. Parietal involvement was related to the visual-motor component with more

anterior portions of IPS being related to the motor production and more posterior portions being related to visual feedback for the purposes of motor production.

In what follows, we discuss these results in light of previous work and discuss the role of each neural component of the larger sensorimotor system.

Precentral Gyri

The precentral gyri were recruited bilaterally for the broad contrast of letter production compared with fixation. When we isolated the motor component of letter production by contrasting letter production and watching the dynamic visual unfolding of the letter, we found only the left precentral gyrus, not the right. This primary motor region was, therefore, only active during actual letter production and did not respond to the visual information that resulted from letter production. Longcamp et al. (2014) found that the left dorsal precentral gyrus responded more during letter production. As Longcamp et al. (2014) provided real-time visual feedback of the letters as they were being produced, it was not clear whether the left dorsal precentral gyrus was related to the motor movements, the visual presentation of letters that occurred during production, or the use of vision to guide the motor movements. We extend this work by showing that the activation of the left precentral gyrus is specific to motor production. These results are in line with the results of James and Gauthier (2006) that demonstrated that the left precentral gyrus was more active while participants wrote a letter without visual feedback compared to when they imagined a letter. They are also in line with work indicating that the left precentral gyrus is involved with the execution of movements, in general (for review: Chouinard & Paus, 2006; Graziano, 2006; Meier et al., 2008; Schieber, 2001).

Superior and Middle Frontal Gyri

The only comparison that revealed a response in any dorsal premotor region was the comparison between letter production and fixation. Neither the motor component nor the visual component contrasts revealed activation in dorsal premotor cortex. We interpret these findings to indicate that the dorsal premotor response in posterior superior frontal sulcus was both motor and visual in nature. We suggest that the motor processes that might occur in this region are mediated by visual feedback during letter

production, perhaps through parietal connections.

We interpret the response in the left superior frontal sulcus during letter production to be analogous to the graphemic-motor frontal area (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009). As such, we would expect this response to be related to serial motoric processing, holding a perceptual representation in a buffer for the purpose of manually producing it stroke-by-stroke, as it occurs during letter production (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009). We found some support for this idea. We found that the left superior frontal sulcus was more active when participants wrote letters without ink (serial motoric processing) than when they watched a statically presented typed letter. We also found, however, that the left superior frontal sulcus was more active when participants watched a letter dynamically unfolding (serial visual processing) than while watching a statically presented typed letter. These results suggest that the left posterior superior frontal sulcus is related to serial motoric processing but remains sensitive to serial visual processing. This suggestion is consistent with the absence of activity in this region for all of our contrasts besides the comparison between letter production and fixation and fits nicely with prior work demonstrating the involvement of dorsal premotor cortex for serial motoric (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009) and visual (Nakamura et al., 2012) processing during letter production.

Although research on letter production typically focuses on motor sequencing of hand movements, eye-movement sequencing must also occur. The sensitivity to serial visual processing that we found in the left dorsal premotor cortex may be related to the visual sampling of a handwritten letter for the purposes of updating motor movement parameters whether or not an overt motor movement is produced, and can be used, conversely, for the motor sampling of a handwritten form for the purposes of updating eye gaze parameters. This interpretation of the left dorsal premotor cortex's role in letter production is in line with work suggesting that dorsal premotor responses that have typically been attributed to Exner area functions may be strongly related to eye movements that occur during letter production. Yuan and Brown (2015) performed a meta-analysis of studies of handwriting and drawing and found that peak activations in coordinates found for handwriting and for drawing were similar to

those found in a meta-analysis of saccadic eye movements (Grosbras, Laird, & Paus, 2005). They, therefore, suggested that premotor responses during handwriting might be tightly linked and, perhaps synonymous, with the frontal eye fields (Yuan & Brown, 2015; but see Matsuo et al., 2003).

Eye movement sequencing naturally co-occurs with hand and finger movement sequencing during letter production and, indeed, both are serial processes that likely support each other. Prior work has shown that activation in left posterior superior frontal sulcus is associated with the serial conversion of a grapheme, a stored perceptual representation of a letterform, into the step-by-step motor commands necessary to recreate the letter using pen and paper (Pattamadilok et al., 2016; Planton et al., 2017; Roux et al., 2009). We extend this work by demonstrating that this serial processing may have some relationship to the serial visual sampling that naturally co-occurs with hand movements during letter production. Further work is needed to disentangle whether the response that we found in left posterior superior frontal sulcus for serial visual processing is related to the coordination of eye movement and finger movement sequencing during letter production or is, instead, related to the serial conversion of a stored letter representation into the sequencing of motor commands required for letter production.

Bilateral Cerebellum

Cerebellar involvement, particularly the cerebellar lobe ipsalateral to the hand used to write, is very consistently reported in studies of handwriting as being related to the motor component of letter production (for a meta-analysis see Planton et al., 2013) although the cerebellum has also been attributed cognitive and linguistic functions (Stoodley & Schmahmann, 2009). We found a bilateral cerebellar response that was weighted more heavily to the right hemisphere for only the motor contrast. We interpret this cerebellar response to be related to hand movements performed during the Write With Ink task that were not necessary during the Watch Dynamic task. This interpretation is consistent with a vast literature relating ipsalateral cerebellar involvement (relative to the effector) to sensorimotor execution processes (Manni & Petrosini, 2004), even for the fine motor movements required for written form production (Baillieux et al., 2010; Haggard, Jenner, & Wing, 1994; Mariën et al., 2009; Planton et al., 2013). More work is necessary to determine the exact role of the cerebellum in this sensorimotor execution process and

the possibility that the cerebellum may also be performing additional cognitive and linguistic processes (Manto et al., 2012; Stoodley & Schmahmann, 2009).

Parietal Cortex (IPS)

The intraparietal sulcus (IPS) has long been associated with visually guided action (e.g., Goodale & Milner, 2005; Milner & Goodale, 2006). As such, it is thought to be a region that combines and integrates visual information in real time for the purpose of supporting motor actions. Prior work suggests that the involvement of parietal cortex in the visual and motor components of writing and drawing is graded, such that more anterior portions of IPS are related to the motor component and more posterior portions are related to the visual component (Haar et al., 2015; Kadmon Harpaz et al., 2014; Thaler & Gooodale, 2011; Yuan & Brown, 2014). We found a similar pattern with the visual and motor components of letter production in the current study and found, further, that an area of overlap between motor and visual components existed in left posterior IPS. Left *anterior* IPS was only associated with the motor component of letter production, whereas the conjunction analysis revealed that the left *posterior* IPS was associated with both visual and motor components of letter production. Indeed, left SPL and left anterior IPS did not demonstrate more activation for any of our other contrasts that were designed to look at responses associated with the different visual percepts produced as a result of letter production.

The role of the left *posterior* IPS in processing the visual percepts that result from–or that guide–the motor production of forms is further demonstrated by its response during purely visual tasks that involve motorically produced percepts. That is, when we compared the perception of handwritten forms to typed forms we found recruitment of the left posterior IPS. This same contrast in previous work only showed recruitment of the frontal cortex (which we do not replicate) (Longcamp et al., 2006, 2011). We believe that these two seemingly contradictory results provide an interesting insight on the nature of perceiving letters and the motor responses that this perception invokes. For instance, Longcamp et al. (2011) used fMRI to compare the perception of lower-case cursive letters to typed letters and found greater frontal motor cortex activation to cursive letters than typed letters. This finding was interpreted as demonstrating that cursive letters invoke a generalized motor plan during visual perception. Behavioral

work supports this interpretation. Individuals can infer motor production steps from simply viewing a letter or word produced in cursive font (Babcock & Freyd, 1988; Freyd, 1987; Orliaguet et al., 1997). When we compared handwritten (printed, not cursive) letters to typed letters, however, we did not find motor cortex activation, but rather recruitment of the left IPS and right ventral temporal cortex. We hypothesize that this seemingly discrepant result actually fits well with previous interpretations in that the perception of *one's own* produced form may not activate generalized motor plans, but rather it may reactivate individual visually-guided action events based on exemplar perception.

Support for this interpretation comes from a long history of research on the differences among frontal motor systems and parietal motor systems (for review: Rizzolatti et al., 1998). The motor plans in the frontal cortex are created from the experiences of acting, and perceiving actions, and are thought to be generalized from numerous instances throughout a lifetime. As such, they are flexible and can be used in many different situations to facilitate motor interaction. In contrast, the motor information in parietal cortex, and more specifically in IPS, is more specific to individual visually guided action events and pairs the motor information with a specific visual percept and, perhaps, prior kinesthetic percepts. This pairing can be re-activated through associative mechanisms (as in viewing one's own handwritten letter) but may not be stored for use in subsequent generalized behaviors because the association is too specific to a particular visually guided event (Goodale & Milner, 2005; Milner & Goodale, 2006). Support for this suggestion comes from prior work that suggests a fronto-parietal system associated with the motor production of written forms (for review: Nakamura & Kouider, 2003) as well as other contrasts in the present study.

Furthermore, we found that there was no difference between the condition where participants perceived their own handwritten letter unfold over time compared with perceiving a static, handwritten version of that same letter. We infer from this that both types of percepts are associated with the prior visually guided production of the letter and therefore will not show differential activation in the IPS. Indeed, when we compared the perception of their own handwritten letter unfolding over time with a static, typed version of the same letter, we saw bilateral frontal (middle frontal gyri) and parietal

(intraparietal sulcus) responses.

More direct comparisons among self-produced handwriting and various other versions produced by oneself and others would be necessary to make strong conclusions based on these results. There is prior work, however, that can offer some additional support. In a study that compared visual perception of handwritten letters that were not written by the participant to typed letters, no parietal activation was found (Longcamp et al., 2011). Dufor and Rapp (2013) found, similar to Longcamp et al. (2011), that parietal cortex demonstrated non-significant sensitivity to letter shape, case, or identity. The handwritten stimuli in both of these studies were not written by the participant themselves and a parietal response was not found in either study. This fits nicely with our suggestion that the parietal response during passive perception was related to the perception of the unique output from a unique visual-motor experience.

Finding parietal activation for visual perception of letters is, nonetheless, a novel finding that suggests that parietal cortex might have some 'memory' for objects—at least objects with which we have a visual-motor history. Traditional accounts of the dorsal visual stream suggest that the visually guided actions mediated by parietal cortex are completely online and do not use stored information (Milner & Goodale, 2006), although more recent accounts suggest that the dorsal stream can be further divided into a dorsal-dorsal stream and a ventral-dorsal stream (Rizolatti & Matelli, 2003). Of these two, the ventral-dorsal stream has potential for 'memory' as it shares many characteristics with the ventral visual stream that is thought to have long-term storage capabilities for such things as object identity (Milner & Goodale, 2006). Our study differed from prior work in that participants' handwritten letters were presented back to them within the same experimental run that they had written them. It may be that the 'memories' in parietal cortex for these specific visual cues are relatively short in comparison to, for example, the memory for object identities in ventral-temporal cortex (Dufor & Rapp, 2013; Rothlein & Rapp, 2014) and may, in having any memory at all, rely upon ventral-dorsal stream mechanisms.

Ventral Temporal Cortex

The visual component of letter production (Write With Ink > Write Without Ink) recruited the ventral temporal cortices bilaterally. This is not surprising given the substantial amount of research on the

involvement of ventral temporal cortex in letter perception (James et al., 2005; James, 2010; James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; Kersey & James, 2013; Longcamp et al., 2003) and letter production (Dufor & Rapp, 2013; James & Gauthier, 2006; Longcamp et al., 2014; Planton et al., 2017). The present finding specifies the role of the left ventral temporal cortex during letter production by demonstrating that it is only recruited during the visual components of letter production. Moreover, we found a greater involvement of the right ventral temporal cortex not only in the visual component of letter production, but also in several of our other contrasts.

Prior work has not typically reported right ventral temporal involvement during letter production. We hypothesize that this may be due to a difference in methodologies between prior work and the present study. In the present study, participants were able to see what they were writing as they were writing it whereas prior work has not typically provided visual feedback during letter production. Only one other study, Longcamp et al. (2014), has studied letter production with visual feedback of the form being created. They found, as did we, a response in right ventral temporal cortex for letter production. They also found this response for digit production, however, and based on additional analyses concluded that this response was likely involved in lower-level effects that would vary between writing instances. One such variation could be the use of visual cues to guide motor movements.

We suggest that the right ventral-temporal response for the motor component may be related to the use of subtle variations in the letterform being produced that may be used during letter production. It is the nature of the fine motor system that each production of a given letter will be slightly different, even in proficient writers, so that each time a letter is written it is essentially in a new ‘font’. The right ventral-temporal response may, accordingly, reflect the detection of instance variability and is in line with findings that link the right fusiform gyrus to the perception of font variations (Barton et al., 2010a; Barton et al., 2010b; Qiao et al., 2010; Gauthier et al., 2000; Rothlein & Rapp, 2014). This interpretation is supported by our other findings: that the right fusiform gyrus responded more during the perception of one’s own handwritten letters than for typed letters, that it did not respond stronger for dynamically unfolding handwritten letters compared to static handwritten letters, and that it responded similarly for

both visual and motor components of letter production. The role of the right fusiform gyrus in letter production may, therefore, be related to the detection or use of subtle visual cues that are suggestive of motor movements, whether this is occurring during the production, or not.

Conclusion

The results of this experiment provide preliminary evidence for the claim that functional connections between visual and motor systems support letter production. Here, we have decomposed letter production into motor, visual-perceptual, and visual-motor components and related these behavioral components to relatively distinct neural sub-systems within the widespread neural system that supports letter production (James & Gauthier, 2006; Longcamp et al., 2014). Each component can be coarsely related to activation in different cortical areas. The L dPrG, L FuG, and left posterior IPS are differentially involved in the motor, visual-perceptual, and visual-motor components of letter production, respectively. We now turn to evaluating (1) the functional connectivity patterns amongst these regions to demonstrate that a functional network comprised of brain regions associated with the motor, visual-perceptual, and visual-motor components supports letter *production* and (2) the relationship between this putative functional network and the functional network that supports letter *perception* in Chapter 4.

CHAPTER 4:

AN ANALYSIS OF THE FUNCTIONAL CONNECTIONS INVOLVED WITH PRODUCING LETTERS BY HAND

Chapter 2 demonstrated that functional connections between ventral-temporal, parietal, and frontal motor cortices supported letter *perception* in preliterate children after letter production training. We proposed that the observed functional connections were a re-engagement of the neural processes that supported the children's prior experience with those letters—that this functional connectivity pattern supported letter perception because it first supported letter production. We did not know, however, that functional connections amongst these neural regions do, in fact, support letter production. To this aim, we first evaluated the activation patterns found during letter production in literate adults in Chapter 3 and, here, we evaluate functional connectivity patterns amongst these regions during letter production and letter perception in the same adults.

The analysis described in this chapter directly assesses the presence of functional connectivity during letter production and letter perception. It addresses two primary questions: Does functional connectivity among ventral-temporal, parietal, and frontal motor cortices support (1) letter production and (2) letter perception? To measure functional connectivity during letter production and letter perception, we performed a generalized psychophysiological interactions analysis (McLaren et al., 2012; O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012) as in Chapter 2. We predicted that functional connections among ventral-temporal, parietal, and frontal motor cortices would support both letter production and letter perception. Based on the activation patterns found during letter production in Chapter 3, we predicted, further, that functional connections between parietal and frontal motor cortices would be associated with the motor component of letter production whereas functional connections between parietal and ventral-temporal cortices would be associated with the visual component of letter production.

Materials and Methods

All analyses were performed on the data set described in detail in Chapter 3. The stimuli and procedures will, therefore, not be reiterated here.

Preprocessing and Motion Correction

All preprocessing and motion correction procedures were performed as described in Chapter 3. We also performed several additional motion analyses to ensure that the results were not biased by task-correlated motion (Appendix B).

Functional Connectivity Analysis

Seed selection. Generalized psychophysiological interactions (gPPI) analysis is a seed-based functional connectivity method and, therefore, requires that a region of interest in the brain be defined as a "seed" (McLaren et al., 2012; O'Reilly et al., 2012). We selected four seed regions based on anatomical and functional criteria based on the results reported in Chapter 3. Anatomical criteria were met by visually inspecting individual anatomical images and consulting the Talairach Daemon as well as the Duvernoy (1999) human brain atlas. Functional criteria were met based on a standard Fixed Effects Generalized Linear Model that included predictors for all conditions in the stimulation protocol performed on all runs for each individual participant. Activation was required to meet a voxel-wise threshold of $p_{vox} < .05$ to be selected as a seed.

Our first two seeds were placed in regions that demonstrated both motor and visual properties in Chapter 3 and, therefore, were most representative of the visual-motor nature of letter production. These two seeds were selected based on the conjunction between the motor (Write With Ink > Watch Dynamic) and visual contrasts (Write With Ink > Write Without Ink). One seed was placed in the left posterior parietal sulcus and another was placed in the right posterior fusiform gyrus. Both seeds were selected in 13 out of 14 participants. Our third seed was placed in the left dorsal precentral gyrus based on the motor contrast (Write With Ink > Watch Dynamic). This seed was localized in 14 out of 14 participants. Our fourth seed was placed in the left fusiform gyrus based on the visual contrast (Write

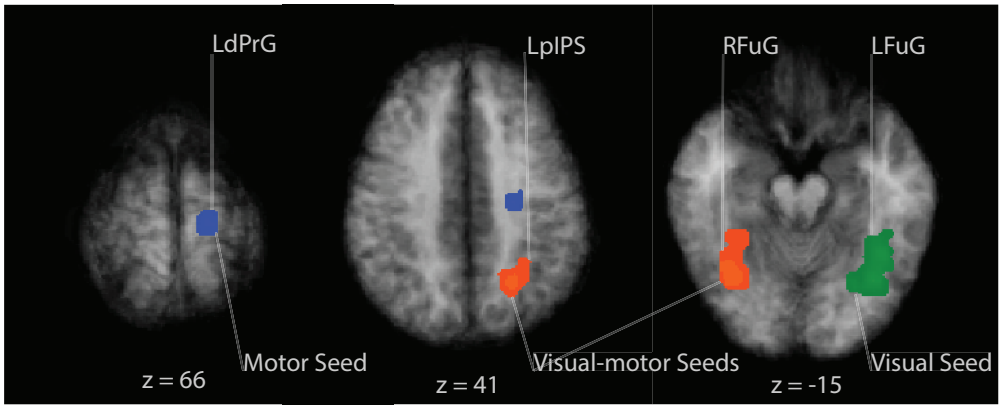

Figure 13. Probability Maps for Four Seeds. All seeds were placed according to functional and anatomical criteria using individual participant functional and anatomical images with a voxel-wise threshold of $p < .05$. A probability distribution map for each seed is overlaid on a group-averaged anatomical image for display purposes. The motor seed is shown in blue. An area in the left dorsal precentral gyrus was selected if its response was greater while writing letters with ink than while watching letters unfold (i.e., the motor component contrast). The visual seed is shown in green. An area in the left fusiform gyrus was selected if its response was greater while drawing letters with ink than while drawing letters without ink (i.e., the visual component contrast). The two visual-motor seeds are both shown in orange. Both seeds were selected in regions that were revealed by the conjunction between the motor and visual component contrasts. These regions included the left posterior parietal sulcus and the right fusiform gyrus.

With Ink > Write Without Ink). This seed was localized in 14 out of 14 participants. Probability maps for all seeds are displayed in Figure 13.

gPPI Analysis. A gPPI model was created for each run and for each seed region. Each model included the standard task predictors (psychological predictors), the demeaned magnitude signal time course from the seed region (physiological predictor), and the element-wise product of each psychological predictor with the physiological predictor (gPPI predictors). The rigid-body motion parameters, spike regressors, and phase regressor were appended to the gPPI design matrix as confound predictors (see *Preprocessing and Motion Correction* in Experiment 2). Random-effects GLM analyses were performed using the full model including all runs for the gPPI contrasts. For each seed, we performed the same five contrasts to determine task-related functional connectivity.

The first two contrasts were designed to investigate functional connectivity related to letter production. The first contrast was designed to identify the functional connections associated with the motor component of letter production and compared functional connections during Draw With Ink to functional connections during Watch Dynamic. The second contrast was designed to identify the functional connections associated with the visual component of letter production and compared functional connections during Draw With Ink to functional connections during Draw Without Ink. The third contrast compared the perception of static, typed letters to a fixation baseline to identify functional connections broadly associated with perceiving letters, as in prior work that has used activation as the dependent measure (e.g., James & Atwood, 2009; Longcamp et al., 2011).

Resulting t-maps were subjected to a voxel-wise threshold of $p_{voxel} = .01$ and subjected to a cluster threshold of 6 contiguous 3 mm isotropic voxels. The voxel-wise and cluster thresholds were more liberal for the functional connectivity analyses than for the whole brain contrasts as reported in Chapter 3 because gPPI functional connectivity analyses have less power than standard Random-effects GLM analyses (McLaren et al., 2012; O'Reilly et al., 2012). Correspondence between anatomical locations and significant activation clusters were determined by, first, referencing the Talairach Daemon and, second,

referencing the Duvernoy (1999) human brain atlas to verify. In cases where the Talairach Daemon and Duvernoy (1999) label disagreed, the Duvernoy (1999) label was selected.

Results

Results are summarized in Figure 14 for brevity and clarity. They are reported in detail below and in Tables 4 through 7.

Visual-motor Seed: Left Posterior Intraparietal Sulcus

The left posterior intraparietal sulcus seed was localized by the conjunction between the motor (Write With Ink > Watch Dynamic) and visual contrasts (Write With Ink > Write Without Ink). This seed demonstrated functional connectivity with bilateral occipital cortices, bilateral lingual gyri, and right fusiform gyrus for the visual contrast and with left posterior IPS for the motor contrast (Table 4). There were no significant functional connections, or trends in that direction, with this seed during typed letter perception.

Visual-motor Seed: Right Fusiform Gyrus Seed

The right fusiform gyrus seed was localized by the conjunction between the motor and visual contrasts. This seed region demonstrated greater functional connectivity with the right posterior IPS, right fusiform gyrus, and left precuneus for the visual contrast and with the right posterior fusiform gyrus, right middle temporal gyrus, and right posterior cingulate gyrus for the motor contrast (Table 5). There were no significant functional connections, or trends in that direction, with this seed during typed letter perception.

Motor Seed: Left Dorsal Precentral Gyrus

The left dorsal precentral gyrus seed was selected based on the motor contrast. This seed region demonstrated greater functional connectivity with three parietal regions, bilateral anterior intraparietal sulcus, bilateral superior parietal lobe, and left cuneus, as well as bilateral precentral gyri in frontal motor cortex and right fusiform gyrus in ventral-temporal cortex, while participants wrote letters with ink compared to when they watched their own handwritten letters unfold (i.e., for the motor component of letter production) (Table 6). This same seed region demonstrated greater functional connectivity with bilateral posterior middle frontal gyri, bilateral posterior cingulate cortex, left posterior intraparietal

sulcus, and bilateral posterior fusiform gyri as well as right middle occipital gyrus while participants wrote letters with ink than when they wrote them without ink (i.e., for the visual component of letter production) (Table 6). There were no significant functional connections, or trends in that direction, with this seed during typed letter perception.

Visual Seed: Left Fusiform Gyrus

The left fusiform gyrus seed was selected based on the visual contrast. Activity in the left fusiform gyrus seed was more correlated with the right lingual gyrus and left fusiform gyrus (posterior to the seed) while participants wrote letters with ink than when they watched their own handwritten letters unfold (i.e., for the motor component of letter production) (Table 7). Activity in the left posterior fusiform gyrus seed was more correlated with activity in left posterior IPS, left fusiform gyrus (posterior to the seed), and right occipital cortex while participants wrote letters with ink than when they wrote letters without ink (i.e., for the visual component of letter production) (Table 7). There were no significant functional connections, or trends in that direction, with this seed during typed letter perception.

Exploratory Analysis: Typed Letter Perception Seeds

We found no significant functional connections during typed letter perception with any of our four seeds. This may have been due to the seed selection criteria. The four seeds were selected because of their involvement in letter production, not letter perception. We, therefore, selected seeds in the left and right fusiform gyrus based on letter perception (as opposed to letter production). These seeds were functionally localized to the left and right fusiform gyri by comparing typed letter perception to fixation, as in previous studies (James et al., 2005; James & Atwood, 2008). The left and right fusiform gyri seeds localized by the traditional typed letter versus fixation contrast were generally more lateral than the left and right fusiform gyrus seeds localized based on the letter production contrasts. We found, again, no significant functional connections, or trends in that direction, for typed letters.

Table 4. Visual-motor Seed: Left Posterior Intraparietal Sulcus

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
			Peak x	*Peak Y*	*Peak z*	*Peak T*	
Motor Component: Write With Ink > Watch Dynamic	1	1221	-36	-55	25	4.99	Left posterior intraparietal sulcus
Visual Component: Write With Ink > Write Without Ink	5	1250	36	-61	7	5.67	Right middle occipital gyrus
		362	36	-70	-17	4.28	Right fusiform gyrus
		338	15	-79	-20	4.88	Right lingual gyrus
		883	-18	-79	-20	5.07	Left lingual gyrus
		527	-36	-82	-11	5.34	Left inferior occipital gyrus

Table 5. Visual-motor Seed: Right Fusiform Gyrus

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
			Peak x	*Peak Y*	*Peak z*	*Peak T*	
Motor Component: Write With Ink > Watch Dynamic	3	3284	54	5	-14	5.27	Right middle temporal gyrus
		5610	27	-61	22	7.26	Right posterior cingulate gyrus
		3760	27	-67	-5	5.83	Right fusiform gyrus
Visual Component: Write With Ink > Write Without Ink	3	450	45	-55	-8	4.35	Right fusiform gyrus
		1349	30	-73	40	5.56	Right posterior intraparietal sulcus
		621	-12	-73	40	4.61	Left precuneus

Table 6. Motor Seed: Left Dorsal Precentral Gyrus

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
			Peak x	*Peak y*	*Peak Z*	*Peak T*	
Motor Component: Write With Ink > Watch Dynamic	9	379	39	-37	-17	4.96	Right anterior fusiform gyrus
		545	42	-31	40	4.62	Right anterior intraparietal sulcus
		879	45	-4	52	4.80	Right precentral gyrus
		3105	12	-67	56	7.04	Right posterior superior parietal lobe
			36	-52	53	4.71	Right middle superior parietal lobe
		502	30	-37	40	4.12	Right middle intraparietal sulcus
		593	-12	-70	50	3.95	Left anterior superior parietal lobe
		962	-12	-76	31	4.44	Left cuneus
		504	-36	-19	55	5.37	Left dorsal precentral gyrus
		3173	-42	-28	31	5.55	Left anterior intraparietal sulcus
Visual Component: Write With Ink > Write Without Ink	10	3282	39	-1	46	5.84	Right posterior middle frontal gyrus
		4774	39	-58	-23	5.89	Right fusiform gyrus
		1284	27	-76	37	4.19	Right posterior intraparietal sulcus
		345	33	-86	10	3.64	Right middle occipital gyrus
		644	15	-49	22	8.67	Right posterior cingulate gyrus
		2372	-6	-40	25	5.44	Left posterior cingulate gyrus
		12786	-24	-61	-14	5.40	Left fusiform gyrus
			-27	-73	37	4.01	Left posterior intraparietal sulcus
		479	-30	-43	-11	4.49	Left posterior fusiform gyrus
		1974	-36	2	43	5.56	Left posterior middle frontal gyrus

Local peaks with a T-statistic greater than 4.0 are reported for large clusters that spanned several anatomical locations.

Table 7. Visual Seed: Left Fusiform Gyrus

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
			Peak x	*Peak y*	*Peak Z*	*Peak T*	
Motor Component: Write With Ink > Watch Dynamic	3	409	18	-73	-17	3.79	Right posterior lingual gyrus
		401	9	-64	-11	5.17	Right anterior lingual gyrus
		343	-24	-76	-17	3.89	Left posterior fusiform gyrus
Visual Component: Write With Ink > Write Without Ink	2	471	36	-85	-9	4.68	Right inferior occipital gyrus
		181	-27	-58	31	4.02	Left posterior intraparietal sulcus
		339	-22	-79	-23	3.89	Left posterior fusiform gyrus

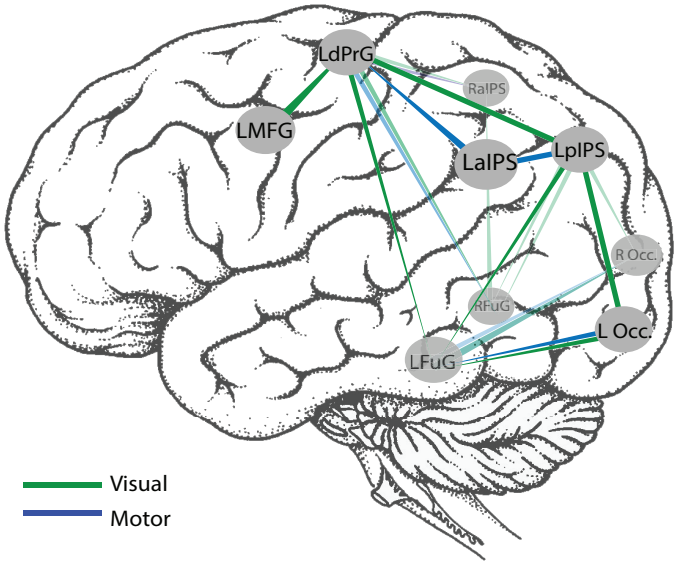

Figure 14. Summary of Functional Connectivity Results. Relationship among activation in ventral-temporal, parietal, and frontal motor regions during letter production. Functional connections shown in blue were greater when participants wrote letters with ink than when they saw their own handwritten letters unfolding as if being written (i.e., the motor component of letter production). Functional connections shown in green were greater when participants wrote letters with ink than when they wrote letters without ink (i.e., the visual component of letter production). Regions that would have been connected to this network with only one link are not shown; these include the right middle frontal gyrus, right middle temporal gyrus, right posterior cingulate cortex, right posterior intraparietal sulcus, right superior parietal lobe, and right precentral gyrus in the right hemisphere and left cuneus, left precuneus, left superior parietal lobe, and left posterior cingulate cortex in the left hemisphere. L Occ. and R Occ. labels encompass all gyri within the occipital lobe. Note that differences in line widths, label sizes, and transparencies are to give the illusion of perspective and are not intended to indicate edge or node weights.

Discussion

We evaluated the presence of functional connections amongst ventral-temporal, parietal, and frontal motor cortices during letter production and perception in literate adults. Our results demonstrate that functional connections among frontal, parietal, and ventral-temporal cortices support letter production. We found, however, no evidence for functional connectivity during typed letter perception.

Functional Connectivity During Letter Production

Our specific predictions were based on the results of the experiment reported in Chapter 3: frontal-parietal connections would be associated with the motor component of letter production while ventral-temporal-parietal connections would be associated with the visual component of letter production. We found, in line with our predictions, that letter production was supported by a functional network comprised of ventral-temporal, parietal, and frontal motor cortices and that the fronto-parietal connections were associated with the motor component of letter production. The visual component of letter production was supported by ventral-temporal-parietal connections, as predicted, but also by a functional connection between the L FuG in ventral-temporal cortex and the L dPrG in frontal motor cortex.

The functional connection between L FuG and L dPrG during letter production is interesting in light of the results of the experiment described in Chapter 2 that demonstrated an increase in functional connectivity between these two regions during letter perception in preliterate children after letter production practice. Our interpretation of the L FuG – L dPrG functional connection during letter perception in Chapter 2 was that it was a re-engagement of the neural systems used during letter production. Finding functional connectivity between L FuG and L dPrG during letter production supports our original interpretation that this functional connectivity pattern supports letter perception because it first supported letter production. It also supports the notion that perceptual processes in ventral-temporal cortex may communicate with frontal motor regions during letter production.

Functional Connectivity During Letter Perception

We expected that functional connections observed during letter perception would be similar to those found during production in literate adults. We found, contrary to our expectations, no evidence for

functional connections during typed letter perception. We were, therefore, unable to directly compare the functional networks supporting letter perception with those that were found to support letter production. This indicates that the functional connectivity observed between the L FuG and the L dPrG in preliterate children after letter production practice (Chapter 2) was not characteristic of the adult response to typed letters. Finding no evidence of functional connectivity during letter perception in literate adults suggests that functional connectivity during letter perception may not support the gains in letter recognition that typically follow letter production practice (Longcamp et al., 2005; Zemlock et al., 2018).

Conclusion

What is the relationship, then, between the emergence of visual-motor functional connectivity during perception and gains in visual recognition? One possibility is, of course, that functional connectivity during visual perception is epiphenomenal—that it contributes in no way to recognition processes and is, instead, simply an artifact of prior experiences. In line with this possibility, the current experiment suggests that functional connections are not necessary for recognition because, presumably, literate adults were able to recognize the letters presented to them. We propose, however, that functional connectivity during visual perception is *not* epiphenomenal. To provide support for the proposal that functional connectivity during visual perception is not epiphenomenal—that it contributes in some way to visual perceptual processes—the following two chapters investigate two possible, non-mutually exclusive relationships between the emergence of visual-motor functional connectivity during visual perception and changes in visual perception.

First, visual-motor functional connectivity during visual perception may only be present during the early stages of learning. Functional connectivity may be a way to integrate information from multiple modalities for the purposes of recognition before processes in the preferred modality are sufficient in and of themselves. If this were the case, then the process of learning should be characterized by functional connectivity that gradually decreases as recognition increases. Such a progression has been documented in motor skill learning (Andres et al., 1999; Bassett et al., 2015). Adults learning a novel visual-motor finger sequence demonstrated greater functional connectivity between primary visual and motor brain

regions during the early stages of learning to perform the sequence compared to later stages when the sequences were over-learned (Basset et al., 2015). A similar trend was found using EEG: frontal motor and parietal activity became less correlated as performance on a finger sequencing task increased (Andres et al., 1999). Neuropsychological case studies provide further evidence for a progression toward more independent, localized functioning. Patients with total commissurotomies demonstrate impaired acquisition of novel bimanual movements with preserved ability to perform bimanual movements that had been acquired prior to the commissurotomy (Sperry, 1968). As far as I am aware, there has been no work on the progression of functional coupling in perceptual learning following sensorimotor training.

This possibility—that functional connections only support the early stages of learning—would appear to be at odds with the findings of the current study. This possibility would predict that letter *production* would not be supported by visual-motor functional connectivity in literate adults for whom, presumably, letter production was an over-learned skill. The current study reports the contrary—that visual-motor functional connectivity supported letter production in literate adults. We note, however, that the current study made use of an fMRI compatible table that may not have been ecologically valid. Participants, for example, could not see their hand as they were producing the letters. Participants in this experiment may not have been able to rely on their preferred modalities as they normally would and, therefore, demonstrated a neural response that was characteristic of an earlier stage of learning (i.e., greater functional connectivity). Literate adults may not need multimodal information during letter production under normal circumstances but may be able to recruit this information when needed. Whether visual-motor functional connections support letter production in only the early stages of learning or through all stages, the findings from the current study are not necessarily at odds with the possibility that functional connections are characteristic of the early stages of learning.

Second, visual-motor functional connectivity during perception may only be present shortly after production practice. Functional connectivity during letter perception may be the result of reverberating activity from the production episode that may (or may not) directly support recognition, as hypothesized in Chapter 2. If this were the case, then increases in functional connectivity during letter perception

immediately after training should be less pronounced after a period of no training. Such a developmental trajectory would be predicted by Hebbian theories of learning that propose that experiences leave behind a residue of reverberating activity that gradually decreases with time (Hebb, 1949; Alvarez & Squire, 1994).

The potential role of these reverberations in neural representation is debated, however. Some theories propose that these reverberations are the neural representation responsible for recognition (McClelland et al., 1995; Versace et al., 2009) while others propose that they merely contribute to the development of other neural processes that eventually become the neural representation (Amit & Brunel, 1995; Freeman, 1995). Results from the current study provide evidence against the idea that reverberations are, themselves, the neural representation, because they suggest that when recognition is at its highest, reverberations are at their lowest.

I, therefore, propose that functional connectivity *indirectly* supports recognition by contributing to the development of some other neural mechanism that supports recognition. Reverberating activity may, for instance, contribute to the development of more localized circuitry (Amit & Brunel, 1995; Freeman, 1995) or some other process entirely. This relationship would be predicted by the results of the current study that suggest that literate letter perception is not supported by functional connectivity. It would also be predicted by theories of memory consolidation (i.e., learning) that suggest that the mechanisms of long-term memory are qualitatively different than short-term mechanisms, though not necessarily unrelated (Aizawa et al., 1991; Amit, 1995; Dayan & Cohen, 2011; Frankland & Bontempi, 2005; Freeman, 1995; Makino et al., 2016).

These two possibilities—that functional connections are only present during the early stages of learning and/or only shortly after training but contribute, nonetheless, to the development of recognition—are consistent with the proposition that functional connectivity is not epiphenomenal to recognition processes. The following two chapters investigate these two non-mutually exclusive relationships between the emergence of visual-motor functional connectivity during visual perception and gains in visual recognition. Chapter 5 investigates the neural systems that support letter perception at

different stages of literacy development using a cross-sectional approach. This experiment addresses the developmental trajectory of more localized processing by assessing the progression of the neural systems that support letter perception at different stages of learning. Chapter 6 investigates the relationships among functional connections among visual and motor neural systems and letter recognition immediately after training and after a no-training delay.

CHAPTER 5:

VISUAL EXPERIENCES DURING LETTER PRODUCTION CONTRIBUTE TO THE DEVELOPMENT OF THE NEURAL SYSTEMS SUPPORTING LETTER PERCEPTION

Producing letter forms by hand changes perceptual processing of those same forms in young children more than other forms of learning (James, 2010; James & Engelhardt, 2012; Kersey & James, 2013). It is still not known, however, why writing by hand has this effect on subsequent visual processing. Numerous studies have demonstrated that learning through self-generated actions is particularly influential in promoting developmental changes in visual object recognition in many different domains (e.g., Bertenthal & Von Hofsten, 1998; Bushnell & Boudreau, 1993; Craddock et al., 2011; Christou & Bülthoff, 1999; Fan et al., 2017; Harman et al.,1999; James et al., 2001; Longcamp et al., 2005; Needham, 2000; Rovee-Collier et al., 1980). While the performance of the action itself may be a part of these developmental changes, the visual percepts that result from these actions may also play a crucial role in the formation of brain systems that process the learned stimulus in subsequent encounters. Two-dimensional objects, such as written symbols, are often created by self-generated actions (i.e., letter production) that present the visual system with exemplars that may form the perceptual information that is stored for those symbols and, in turn, effect subsequent visual processing. Here, we contend that the results of letter production—the forms that are then perceived by the visual system—are important drivers of developmental change in both the dorsal motor system and the ventral-temporal cortex.

Though experience producing letters by hand increases activation in both dorsal motor systems and ventral-temporal cortex during letter *perception* relative to other motor actions with letters (e.g., typing) (James & Atwood, 2009; James & Engelhardt, 2012; Kersey & James, 2013), the mechanisms underlying changes in the dorsal motor system may differ from the mechanisms underlying changes in the ventral-temporal cortex. Changes in the dorsal motor system may be most associated with the activity that is evoked in this system during the execution and real-time monitoring of the motor movements required to produce a symbol by hand. The frontal motor system may store general motoric experiences (e.g.,

motor programs) while parietal cortex may participate in the real-time guidance required to successfully implement these general motor plans in different contexts. Changes in ventral-temporal cortex, on the other hand, may be more associated with the visual experiences with that symbol that result from the production episode (e.g., a handwritten symbol) than the motor experience, specifically. The information processed in the dorsal motor system during letter production is, therefore, qualitatively different than the information processed in the ventral-temporal cortex and such differences are likely to also be relevant to the neural processing that occurs in these regions during letter perception.

Present Study

The purpose of this study was to better understand the developmental progression of the neural system that supports letter perception among children in the very early stages of learning about letters, children in later stages, and in literate adults. Our primary goal was to characterize the developmental trajectory of more localized neural responses to letters to provide some information concerning the changes in local processing that might occur throughout learning. The results of Chapters 2 through 4 suggest that functional connectivity may indirectly support recognition by contributing to the development of some other neural mechanism that supports recognition. Functional connectivity may be a way to integrate information from multiple modalities for the purposes of recognition before processes in the preferred modality are sufficient in and of themselves. Visual-motor functional connectivity was present in preliterate children during letter perception (Chapter 2) but not in literate adults (Chapter 4), suggesting that visual-motor functional connectivity and visual recognition are inversely related: less functional connectivity is associated with better recognition, greater functional connectivity is associated with worse recognition. Here, we supplement these findings with a characterization of the developmental progression of more localized processing in visual-perceptual, visual-motor, and motor neural systems.

We also sought to provide additional context to the development of neural systems supporting letter perception by evaluating neural responses to the visual inputs created during letter production in each group. The development of more localized processing in visual-perceptual, visual-motor, and motor neural systems may be more related to the specific visual-perceptual, visual-motor, and motor experiences

than any developmental effects that might stem from functional connectivity. It is, therefore, important to determine the neural effects of the visual-perceptual experiences with letters that are created during letter production to evaluate the degree to which visual experiences with letters that are produced during letter production may be driving developmental changes in localized processes.

We investigated, first, the neural systems that support the perception of stereotypical letters (i.e., typed letters) to identify the neural system that supports typical letter perception, as in prior work (James, 2010; James & Atwood, 2009; James & Engelhardt, 2012; James & Gauthier, 2006; Kersey & James, 2013; Longcamp et al., 2003). Our goal was to characterize the progression of letter-sensitive neural responses to provide support for the notion that developmental changes in more localized processes occur as letter recognition abilities increase. We, therefore, evaluated differences in the neural responses that supported early- and late-stages of letter learning by evaluating neural activation differences among early-literate children, literate children, and literate adults during typed letter perception.

We then investigated the neural systems that respond to the different visual experiences of letters produced during letter production, as in Chapter 3. These visual experiences included the unfolding of a letter as it is being produced as well as the final, static handwritten letter. Both visual experiences were the participant's own productions. We also included static handwritten letters that were produced by an age-matched control to control for authorship/ownership effects. Our analyses identified differences within and between groups in the neural responses to the different visual experiences that result from letter production. We expected that the neural responses to the visual experiences that result from letter production would demonstrate different responses in dorsal and ventral systems based on experience. We expected, specifically, an experience-dependent shift towards response to category in ventral-temporal cortex and towards the presence of movement cues in the dorsal motor system.

It would have been ideal to also characterize the developmental trajectory of the patterns of functional connectivity, themselves. Cross-sectional comparisons of functional connectivity, however, are plagued by age-related motion confounds (Power et al., 2012; Satterthwaite et al., 2012, 2013). Although task-based functional connectivity methods are more robust to motion confounds (Vinci-Booher, James,

& James, 2015), group differences in motion estimates larger than a few milli-meters may still present issues. We, therefore, were unable to characterize the developmental trajectory of functional connectivity during letter perception in this study.

Materials and Methods

Participants

Children (4.5 - 8.5 yrs., n = 41) were recruited through an in-house database of parents in the local community and through word-of-mouth. Parents provided written informed consent and were compensated with a gift card. Children who were 7 years or older provided written informed assent. All children were compensated with a small toy or gift card. Adult participants (21 - 25 yrs., n = 15) were recruited through an in-house database and through word-of-mouth. Adult participants provided written informed consent and were compensated with a gift card. All participants were screened for neurological trauma, developmental disorders, and MRI contraindications. All participants were right-handed with English as their native language.

Three children were excluded due to difficulty writing on the tablet during the MRI (e.g., slower than 4 seconds, not drawing between trials and/or blocks) and/or technical problems with the functioning of the tablet (e.g., cable attachment was damaged). Data from one child were lost in a technical error from the MRI facility. Four adults and none children were excluded due to an unacceptable amount of motion during the MRI scanning procedure. We, therefore, obtained useable fMRI data from 11 adults and 27 children. The 13 youngest children were assigned to the younger age group and the 14 oldest children were assigned to the older age group.

Apparatus and Stimuli

Apparatus. The MRItab and cage are displayed in Figure 15 (for a full description see Vinci-Booher, Sturgeon, James, & James, 2018). The MRItab makes use of a touchscreen surface placed atop a novel MR-safe video-display screen and allows visually-guided interaction with the display by virtue of tilting the head slightly and placing the monitor box above the lap of the participant. All stimuli were recorded and presented using the MRItab. Auditory instructions and letter prompts were presented

through MR-safe headphones. Boom™ was used to enhance audio clarity. An in-house Matlab program using the Psychophysics Toolbox extensions interfaced with the MRItab and headphones to record and present all stimuli (Brainard, 1997; Pelli, 1997). Participants wore a Wheaton® elastic shoulder immobilizer to reduce motion and inflatable head immobilization padding was used in the head coil. Children wore MRI-compatible headphones in the MRI for safety and stimuli presentation reasons.

Stimuli. A set of 12 single upper case letters of the Roman alphabet were selected: A, B, C, D, G, H, J, L, Q, R, U, and Y. Pilot testing indicated that these 12 letters were the best combination of letters that the youngest of our children would likely know and be able to write within a reasonable time frame and whose names would not be easily confused (e.g., "c" and "e").

All stimuli were presented/produced in white on a black background. A box that subtended 10 by 10 degrees of visual angle was displayed on the tablet at all times. A singular dot was presented in the center of the screen during the initial and final fixations. Stimuli presented within the box changed according to condition.

Although the full experiment included 8 conditions, we analyze only 4 here that pertained to letter perception: Watch typed letter, watch handwritten letter static other, watch handwritten letter static own, and watch dynamic letter. Typed letters were always presented in 120-point Arial font and subtended 4 by 4 degrees of visual angle. Stimuli for the Watch Static Letter Other condition were recorded from age-matched controls. The stimuli in the watch handwritten letter own were previously recorded (within same experimental session) productions of the subjects' own handwritten forms. In watch dynamic letter, the participants viewed their own previous production of a letter unfold in real time (previously recorded from same experimental session).

Each block contained six letters. The six letters for each block were selected randomly from the full stimulus set at the beginning of each run, with the restriction that a particular set may not contain letter names that are easily confused (Conrad, 1964; Hull, 1973). Note that in the Watch Dynamic Letter

Figure 15. Experimental Setup. Adults and children used the same apparatus and special care was taken to ensure the comfort of the participants. The MRItab (Vinci-Booher et al., 2018), arm pillow, and Wheaton® elastic shoulder immobilizer were adjusted for each participant. Subject-specific adjustments ensured that the participants were in a comfortable writing position and could see the screen of the MRItab.

Trace, Watch Static Letter Own, and Watch Dynamic Letter Dot conditions participants viewed their own handwritten productions–recorded on the MRItab just before the scanning session. The six letters used for these blocks were necessarily the same set of six letters. For this reason, the same set of six letters was also displayed in the Watch Static Letter Other and Watch Typed conditions.

In all conditions, block instructions and letter names were pre-recorded from a female native English speaker and played at the beginning of each block and trial, respectively. Block instructions were kept to a set of three simple one-word imperatives: “Draw”, “Watch”, and “Touch”. Note that for the purposes of the present analyses, only the ‘watch’ command blocks were analyzed.

Procedure

Children. After the consenting process was completed, Children were first asked to write the 12 single upper-case letters of the Roman alphabet to dictation using the MRItab. This step was necessary for the collection of handwriting samples and in acclimating them to working with the MRItab. It also served as an additional screening criterion. Only children who produced a form to dictation within the allotted 4 seconds for at least 10 of the 12 letters were permitted to continue in the study. We did not require that their production was accurate or legible.

After a short movie in the MRI simulator, children performed an abbreviated version of the stimulation protocol also in the simulator (Figure 16). If they made an error of any sort (e.g., tracing the statically presented letters instead of watching them), they received feedback and were asked to try again. Once it was apparent that they understood their tasks and if they appeared comfortable in the MRI simulator, they continued to the actual MRI environment.

During the initial anatomical scan, children were allowed to watch a movie, listen to an audio book, or simply rest. Following the anatomical scan, each functional run contained a complete set of experimental conditions: 4 motor and 4 perceiving blocks (Figure 16) and lasted 344 seconds (5:44 minutes). We acquired up to four functional runs, depending upon the comfort and compliance of the participant. Block orders were pseudo-randomized and counter-balanced across participants.

Each block within the functional runs contained six 4-second trials. Blocks were separated by 14-

second inter-block intervals, the last two seconds of which were auditory instructions for the following block. Initial fixation and final fixation times were 20 seconds and 10 seconds, respectively. Before each block, auditory instructions alerted the participant as to what would be expected of them throughout the next block.

There were 4 motor blocks that were not analyzed for the current report. During all 4 perceptual blocks, participants heard one letter name per trial and passively perceived a letter that they had written dynamically unfolding, a static version of their own handwritten letter, a static version of a letter written by an age-matched control, or typed letters. The handwritten stimuli used in the perceiving blocks were collected from participants prior to the scanning session.

Adults. The neuroimaging procedure for the imaging session for adults was the same as the procedure for children, except that adults were not required to undergo training in the MRI simulator. Adult participants did however, write 12 upper-case letters of the Roman alphabet (i.e., A, B, C, D, G, H, J, L, Q, R, U, and Y) one at a time to dictation using the MRItab outside of the MRI environment. After this short session, adult participants began the imaging session. The stimulation protocol for the imaging session for adults was the same as the stimulation protocol for children.

Scanning parameters. Neuroimaging was performed at the Indiana University Imaging Research Facility, housed within the Department of Psychological and Brain Sciences with a Siemens Magnetom Prisma 3-T whole-body MRI system. High-resolution T1-weighted anatomical volumes were acquired using a MPRAGE sequence: TI = 900 ms, TE = 2.98 ms, TR = 2300 ms, flip angle = 9°, with 176 sagittal slices of 1.0 mm thickness, a field of view of 256 x 248 mm, and an isometric voxel size of 1.0 mm^3. For functional images, the field of view was 220 x 220 mm, with an in-plane resolution of 110 x 110 pixels and 72 axial slices of 2.0 mm thickness per volume with 0% slice gap, producing an isometric voxel size of 2.0 mm^3. Functional images were acquired using a gradient echo EPI sequence with interleaved slice order: TE = 30 ms, TR = 1000 ms, flip angle = 52° for blood-oxygen-level-dependent (BOLD) imaging.

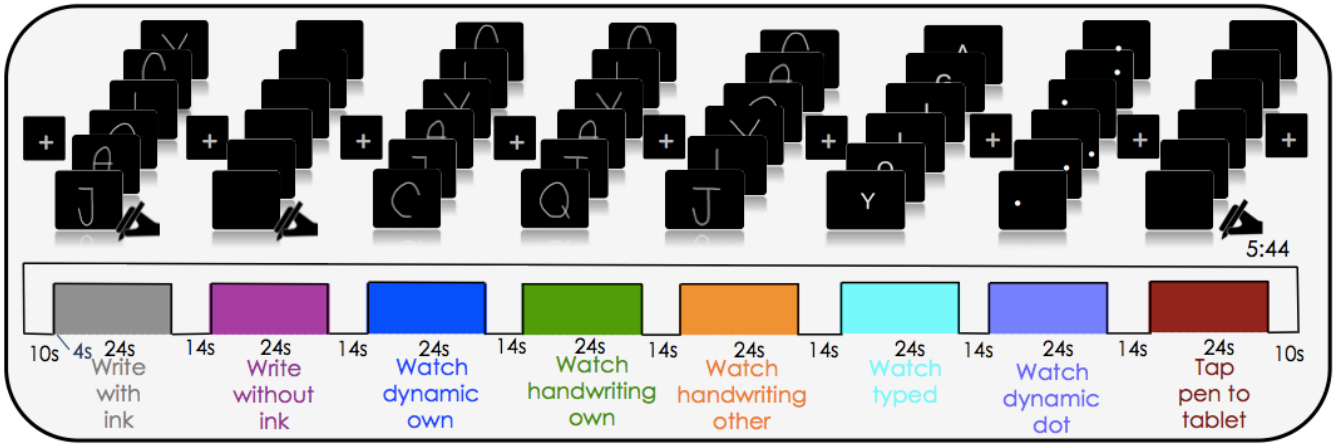

Figure 16. Stimulation Protocol During fMRI Scanning. The figure presents a depiction of the blocks within each run and the trials within each block. Block orders were pseudo-randomized and counter-balanced across runs. The six letters used for each condition within a run were the same set of six letters. Letter orders within a block were randomized. Block instructions and letter names were pre-recorded. Block instructions were played at the beginning of each block to alert participants to the task. Letter names were played at the beginning of each trial to alert the participant to the letter that they should write or to the letter that would be displayed.

Analyses

All neuroimaging analyses were conducted using Brain Voyager QX, Version 2.8 (Brain Innovation, Maastricht, Netherlands).

Neuroimaging Preprocessing. Individual anatomical volumes were normalized to Talairach space (Talairach & Tournoux, 1988). Preprocessing of functional data included slice scan time correction, 3-D motion correction using trilinear/sinc interpolation, and 3D Gaussian spatial blurring with a full-width-at-half-maximum of 6 mm. Temporal high-pass filtering was performed using a voxel-wise GLM with predictors that included a Fourier basis set with a cut-off value of 2 sine/cosine pairs and a linear trend predictor. During normalization, functional data were re-sampled to 3 mm^3 isometric voxels. Coregistration of functional volumes to anatomical volumes was performed using a rigid body transformation. To account for head motion, rigid body transformation parameters were included in the design matrix as predictors of no interest (Bullmore et al., 1999; Weissenbacher et al., 2009) along with spike regressors for each time point at which the relative root mean squared (RMS) time course exceeded 2.0 mm (Satterthwaite et al., 2013; Van Dijk et al., 2012).

Analyses. The statistical analyses began with a voxel-wise general linear model (GLM) with one predictor of interest for each condition and seven predictors of no interest that were included for motion correction purposes only. Each predictor of interest was convolved with a double-gamma hemodynamic response function (Boynton et al., 1996). The resulting design matrix was subjected to a Random-effects GLM analysis for planned contrasts.

We performed several whole brain contrasts within each participant group to observe activation associated with the different visual experiences associated with letter production. Comparing Watch Dynamic Letter Own with Watch Static Letter Own revealed areas associated with seeing a form unfold over time, a contrast that we will refer to as the *unfolding* contrast; comparing Watch Static Letter Own with Watch Static Letter Other revealed areas associated with the perception of one's own handwritten form, the *ownership* contrast; comparing Watch Static Letter Other to Watch Static Letter Typed revealed areas associated with the *perception of handwritten* forms, the handwriting contrast; contrasting Watch

Static Letter Typed with fixation revealed areas associated with the perception of *typed letters*. The resulting t-maps were subjected to a voxel-wise threshold of $p_{voxel} < .01$ with a cluster threshold of 60 contiguous 2-mm isotropic voxels.

We then investigated the interaction between the conditions and the groups with a second level analysis that compared the contrast maps among groups. For each contrast map, we performed a One-way ANOVA at the whole brain level. The analysis proceeded in a voxel-wise fashion, with one model for each voxel that included one between-participant factor, GROUP, with three levels: younger children, older children, and adults. The dependent variable was the voxel's t-value for the contrast of interest. We followed each overall whole brain ANOVA with post hoc between-group comparisons at the whole brain level. Resulting statistical maps for the overall ANOVA and post hocs were subjected to a corrected voxel-wise threshold of $p_{vox} < .001$ with a cluster threshold of 6 contiguous 2-mm isotropic voxels.

Results

Typed Letters

We compared activation during the perception of typed letters to activation during fixation to identify the entire letter processing system, as has been performed in prior work (James & Atwood, 2009; Longcamp et al., 2003, 2011). We found no significant responses during passive typed letter perception in the younger children (Table 8). Both literate groups, older children and adults, demonstrated a response to typed letters (Tables 9 and 10; Figure 17).

Literate adults recruited four major clusters during letter perception (Table 10; Figure 17). The first cluster included left ventral premotor cortex, including posterior middle frontal gyrus and posterior inferior frontal gyrus. The second cluster included left intraparietal sulcus. The third and fourth clusters covered posterior portions of lateral temporal lobe and lateral occipital cortex, extending down into the fusiform gyrus in the left, and right hemispheres respectively. These last two clusters covered regions of cortex often referred to as the lateral occipital complex (LOC). Older children recruited three major clusters, all within ventral-temporal cortex (Table 9) two that were largely consistent with right and left LOC, and the third located in the left fusiform gyrus, anterior to the left LOC response. These results are

consistent with a large number of prior works that demonstrate a similar ventral-temporal and fronto-parietal neural response during passive letter perception in adults (James & Atwood, 2009; James & Gauthier, 2006; Longcamp et al., 2003, 2005, 2006, 2008) and in children with handwriting experience (James, 2010; James & Engelhardt, 2012; Kersey & James, 2013).

The second level analysis indicated significant differences among groups during the perception of typed letters in the left inferior frontal gyrus, left dorsal precentral gyrus, left posterior intraparietal sulcus, left fusiform gyrus, right fusiform gyrus, right occipital cortex, and an anterior portion of the right superior parietal lobe (Table 11; Figure 19).

Post hoc between-group comparisons revealed that the left fusiform gyrus response was greater in the older children than in the younger children, consistent with prior work indicating that the onset of a left fusiform response during letter perception is related to developmental changes in letter recognition ability and writing by hand (James, 2010; James & Engelhardt, 2012; Kersey & James, 2013) (Table 11; Figure 18). The right dorsal postcentral gyrus also was more responsive in the older children than in the younger children during typed letter perception (Table 11). Post hoc comparisons also revealed several responses that were greater in the literate adults than in the younger children, including the left inferior frontal gyrus, left dorsal precentral gyrus, left posterior intraparietal sulcus, and the right fusiform gyrus (Table 11; Figure 19). There were no significant differences between the adults and the older children.

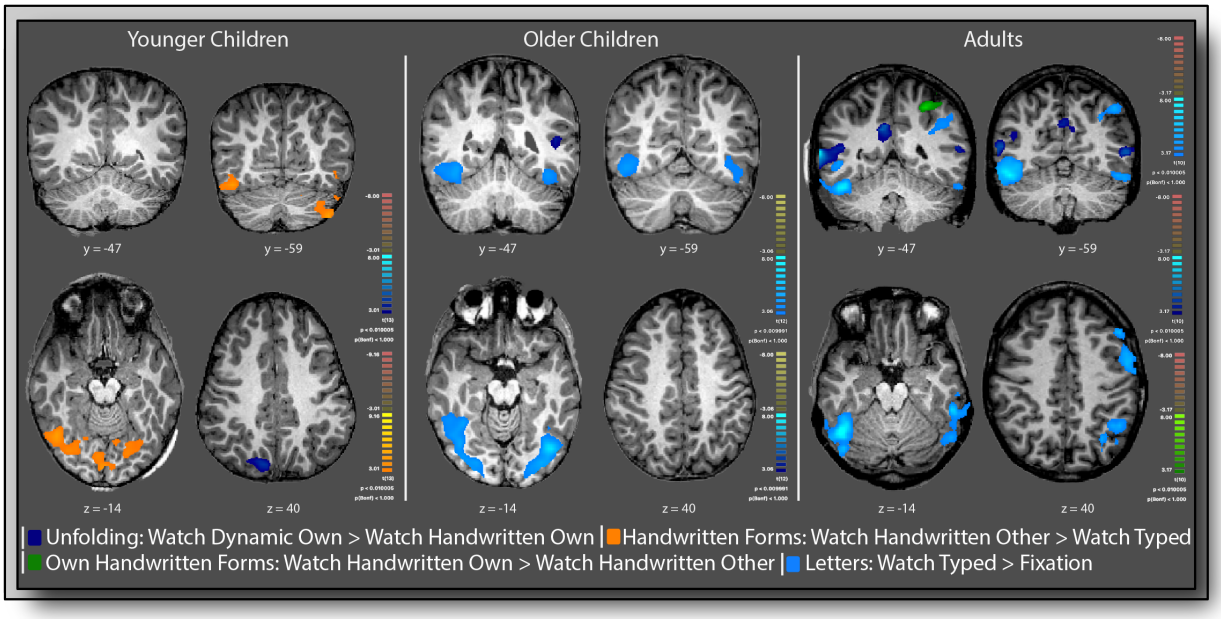

Figure 17. Results of Whole Brain Contrasts for Each Group. Results of all contrasts are presented on a representative participant's brain for each age group. The results of each contrast are displayed in different colors (see figure legend). Younger children (left) responded to handwritten forms (orange) and to the unfolding (dark blue) while demonstrating no response to the perception of typed letters (light blue). Older children (center) and adults (right) responded to typed letters and to the unfolding. Adults demonstrated an additional response to the perception of one's own handwritten forms (green). Talairach coordinates for each slice are displayed. Results are presented a $p_{vox} < .01$ with a cluster threshold of 60 contiguous 2-mm isotropic voxels.

Table 8. Whole Brain Contrasts Within Groups: Younger Children

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates* Peak x	Peak y	Peak z	*Peak T*	*Anatomical Location*
*Watch **Dynamic** Letter Own > Watch **Static** Letter Own*	1	3463	12	-76	37	4.87	Right Precuneus
*Watch Static Letter **Own** > Watch Static Letter **Other***	0	--	-	-	-	-	--
*Watch Static Letter **Other** > Watch Static Letter **Typed***	3	31789	30	-70	10	8.16	Right Posterior Cingulate Cortex
			12	-91	-2	6.69	Right Lingual Gyrus
			-12	-67	16	5.77	Left Posterior Cingulate Cortex
			39	-76	-5	5.72	Right Inferior Occipital Gyrus
			-24	-73	-18	5.17	Left Posterior Fusiform Gyrus
			42	-61	-14	4.73	Right Posterior Fusiform Gyrus
		3811	-27	-76	7	4.15	Left Cuneus
		2433	-42	-55	-41	5.23	Left Cerebellum
*Watch Static **Letter Typed** > Fixation*	0	--	-	-	-	-	--

Local peaks with a T-statistic greater than 4.0 are reported for large clusters that spanned several anatomical locations.

Table 9. Whole Brain Contrasts Within Groups: Older Children

Contrast	*Nbr. Of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
			Peak x	*Peak y*	*Peak z*	*Peak T*	
*Watch **Dynamic** Letter Own > Watch **Static** Letter Own*	1	1684	-42	-43	10	4.65	Left Middle Temporal Gyrus
*Watch Static Letter **Own** > Watch Static Letter **Other***	0	--	-	-	-	-	--
*Watch Static Letter **Other** > Watch Static Letter **Typed***	0	--	-	-	-	-	--
*Watch Static **Letter Typed** > Fixation*	2	9498	39	-64	-12	4.69	Right Fusiform Gyrus
		7367	-42	-70	-13	7.0	Left Fusiform Gyrus

Table 10. Whole Brain Contrasts Within Groups: Adults

Contrast	*Nbr. of Clusters*	*Cluster Size (voxels)*	*Talairach Coordinates*			*Peak T*	*Anatomical Location*
			Peak x	*Peak y*	*Peak z*		
*Watch **Dynamic** Letter Own > Watch **Static** Letter Own*	3	6231	60	-46	10	8.02	Right Middle Temporal Gyrus
		2236	-51	-61	7	7.00	Left Middle Temporal Gyrus
		1718	6	-52	31	5.78	Right Precuneus
*Watch Static Letter **Own** > Watch Static Letter **Other***	1	2030	-27	-46	49	6.90	Left Precuneus, along Intraparietal Sulcus
*Watch Static Letter **Other** > Watch Static Letter **Typed***	0	--	-	-	-	-	--
*Watch Static **Letter Typed** > Fixation*	4	12189	45	-52	-16	9.72	Right Fusiform Gyrus
		5068	-51	8	25	5.90	Left Inferior Frontal Gyrus
			-51	-1	40	5.30	Left Dorsal Precentral Gyrus
			-51	20	34	4.63	Left Posterior Middle Frontal Gyrus
		4290	-54	-37	-17	6.81	Left Fusiform Gyrus
		3332	-45	-55	43	6.04	Left Inferior Parietal Lobe, along the Intraparietal Sulcus

Local peaks with a T-statistic greater than 4.0 are reported for large clusters that spanned several anatomical locations.

Handwritten Letters

Dynamic Unfolding. We compared activation during Watch Dynamic Own to activation during Watch Static Own to identify regions that were more sensitive to the dynamic unfolding of a letter. A response to the dynamic unfolding was present in all groups (Tables 9 – 11; Figure 17). In the younger children, activity in the right precuneus was associated with the perception of the dynamic unfolding. In the older children, activity in the left temporal cortex was associated with the perception of the dynamic unfolding. Adults demonstrated a response to the dynamic unfolding in bilateral temporal cortex, right posterior cingulate cortex, and left posterior middle frontal gyrus. The second level analyis revealed no significant differences among groups (Table 11).

Static handwritten forms. Responses to handwritten forms were identified by comparing activation during the perception of letters written by an age-matched control to typed versions of those same letters. Younger children demonstrated a response to handwritten forms in bilateral ventral-temporal cortex (Table 8; Figure 17). Neither the older children nor the literate adults demonstrated a selective response to handwritten forms (Tables 10 and 11).

The second level analysis revealed a difference among groups in the left posterior fusiform gyrus and in the left intraparietal sulcus (Table 11; Figure 18). Post hoc between-group comparisons revealed that the response in the left posterior fusiform gyrus was greater in the younger children than in the older children. The left intraparietal sulcus response was greater in younger children than in literate adults and there were no significant differences between the adults and the older children.

Ownership. To identify neural regions that had a greater response during the perception of one's own handwritten letters than letters written by an age-matched control, we compared activation during Watch Static Own with activation during Watch Static Other. Neither the younger children nor the older children demonstrated a neural response associated with the perception of one's own handwritten forms (Tables 9 and 10). Literate adults, however, responded to the perception of one's own handwritten letters in left superior parietal cortex along the intraparietal sulcus (Table 10; Figure 17). The second level analysis revealed no significant differences among groups (Table 11).

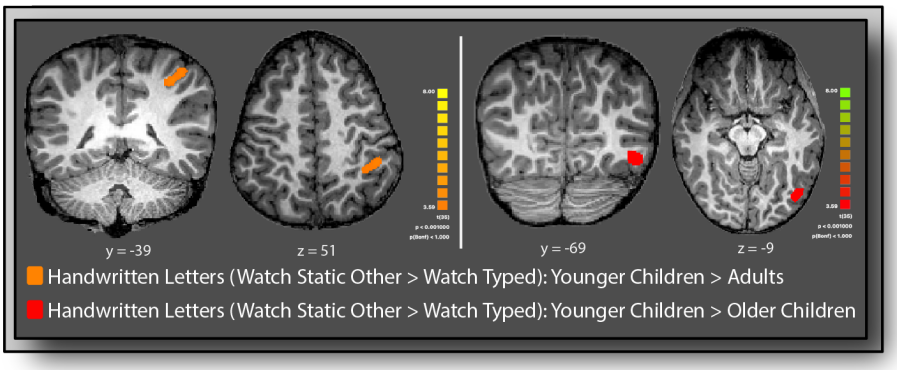

Figure 18. Group Differences for the Perception of Handwritten Forms. A whole brain One-Way Repeated Measures ANOVA revealed that activation in the left posterior fusiform gyrus and the left intraparietal sulcus differed among younger children, older children, and literate adults. Post hoc between-group comparisons indicated that the difference in the left intraparietal sulcus could be attributed to more sensitivity to handwritten forms in the younger children than in the literate adults (orange) and that the differences in the left posterior fusiform gyrus could be attributed to more sensitivity to handwritten forms in the younger children than in the older children (red). There were no differences between older children and literate adults. Talairach coordinates for each slice are displayed. Results are presented a $p_{vox} < .001$ with a cluster threshold of 6 contiguous 2-mm isotropic voxels.

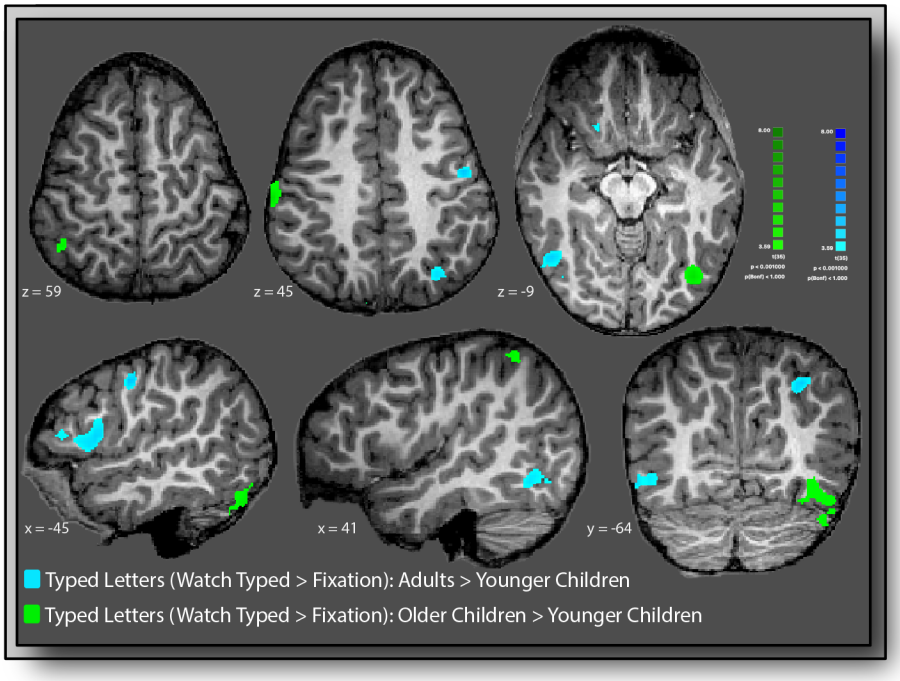

Figure 19. Group Differences for the Perception of Typed Letters. A whole brain One-Way Repeated Measures ANOVA revealed that activation in the left posterior fusiform gyrus, right posterior fusiform gyrus, left posterior intraparietal sulcus, left inferior frontal gyrus, and left dorsal precentral gyrus differed among younger children, older children, and literate adults. Post hoc between-group comparisons indicated that the difference in the left posterior fusiform gyrus and the right dorsal postcentral gyrus could be attributed to more sensitivity to typed letters in the older children than in the younger children (green) and that the difference in the other regions could be attributed to more sensitivity to typed letters in the literate adults than in the younger children (turquoise). There were no differences between older children and literate adults. Talairach coordinates for each slice are displayed. Results are presented a $p_{vox} < .001$ with a cluster threshold of 6 contiguous 2-mm isotropic voxels.

Table 11. **Whole Brain Contrasts Between Groups**

Statistical Map	*Nbr. of Clusters*	Post Hoc Comparison	*Cluster Size (voxels)*	*Talairach Coordinates*				*Anatomical Location*
				Peak x	*Peak y*	*Peak z*	*Peak T*	
Watch ***Dynamic*** *Letter Own* > *Watch* ***Static*** *Letter Own*	0	--	--	-	-	-	-	--
Watch Static Letter ***Own*** > *Watch Static Letter* ***Other***	0	--	--	-	-	-	-	--
Watch Static Letter ***Other*** > *Watch Static Letter* ***Typed***	2	Younger Children > Older Children	612	-48	-67	-10	4.50	Left Fusiform Gyrus
		Younger Children > Adults	267	-39	-40	49	4.50	Left Inferior Parietal Lobe, along
Watch Static ***Letter Typed*** > *Fixation*	6	Adults > Younger Children	1517	-45	11	13	4.81	Left Inferior Frontal Gyrus
		Adults > Younger Children	288	-48	-7	46	4.81	Left Dorsal Precentral Gyrus
		Adults > Younger Children	384	-32	-64	43	4.46	Left Precuneus, along
		Adults > Younger Children	910	48	-58	-9	4.66	Right Fusiform Gyrus
		Older Children > Younger Children	1591	-39	-70	-11	4.90	Left Fusiform Gyrus
		Older Children > Younger Children	540	60	-22	46	5.09	Right Dorsal Postcentral Gyrus

Local peaks with a T-statistic greater than 4.0 are reported for large clusters that spanned several anatomical locations.

Discussion

To better understand how the visual experiences produced during letter production might contribute to developmental changes in localized neural responses to visually presented, stereotypical letters (James, 2010; James & Atwood, 2009; James & Engelhardt, 2012; Kersey & James, 2013), we investigated the neural responses associated with the perception of letters dynamically unfold as if being written, letters that had been handwritten by oneself, letters that had been written by another, and letters in typed font. We investigated these responses in children in the early stages of learning about letters, children in later stages, and in literate adults. By exposing participants to the visual percepts that result from letter production as well as typed letters, we have shown that different types of visual percepts of a single category–letters–recruit different neural systems and that these systems change with experience. Our results make two crucial contributions: (1) Adult-like letter processing emerges earlier in ventral-temporal cortex than in parietal and frontal motor regions. (2) The perception of handwritten forms that occurs during letter production may contribute to this developmental trajectory.

Perception of Typed Letters

A large body of literature has reported letter-selective neural responses in ventral temporal cortex with a focus on sensitivity to letters as an object category in the left fusiform gyrus (e.g., Cohen et al., 2003; Dufor & Rapp, 2013; Flowers et al., 2004; Dehaene et al., 2005; Garrett et al., 2000; Gauthier et al., 2000; James et al., 2005; Rothlein & Rapp, 2014). Neural responses that are greater to letters than other similar objects have also been observed in the posterior parietal cortex, the dorsal and ventral primary motor cortex, and the middle frontal and inferior frontal gyri (James & Atwood, 2009; James & Gauthier, 2006; Longcamp et al., 2003). In the current study, adults recruited this well-known extensive system during typed letter perception (Longcamp et al., 2014; James & Gauthier, 2006; Yuan & Brown, 2014). The older children recruited only the ventral-temporal portion of this neural system and the younger children showed no activation to typed letters compared with fixation. Directly comparing between groups revealed that the fusiform gyrus response was greater in the older children than in the younger

children and, further, that responses that were greater in the literate adults compared to the younger children were predominately located within the dorsal motor system.

Our findings–that only adults recruited the full parietal-frontal system during typed letter perception—suggests that an extensive amount of letter production experience may be required for parietal-frontal regions to develop a localized response during letter perception. We have, nonetheless, found activation in these regions in young children during letter perception after a short amount of within-experiment handwriting training in prior studies (James & Engelhardt, 2012; Kersey & James, 2013). Although not empirically tested yet, we would propose that the small amount of within-experiment training may result in a temporary, short-lived increase in the neural system that supports letter perception. For this response to become stable and permanent, however, more extensive experience with letter production would be required. That the dorsal visual processing stream takes extensive experience to develop a stable response is consistent with work that suggests a more prolonged trajectory for the functional development of the dorsal relative to the ventral visual stream for children in our age range (for review see Stiles, Akshoomoff, & Haist, 2013). It is also consistent with the development of underlying white matter connectivity (Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008) and the general trend found in all of our analyses that the parietal and frontal cortices appear to develop letter selectivity at a later age than ventral-temporal cortex.

Perception of Handwritten Forms

Dynamic unfolding. Our whole brain contrasts revealed a bilateral response in temporal cortices as well as a response in right precuneus in the parietal cortex in literate adults during the perception of a letter dynamically unfolding as if it were being written relative to the final, static versions of those handwritten letters. The bilateral temporal response was near anatomical regions commonly associated motion perception, often referred to as MT/V5 (Tootell et al., 1995; Zeki et al., 1991). The right precuneus has also been associated with motion perception and more specifically with the necessity of directing visual attention for tracking purposes (for review see Cavana & Trimble, 2006). We, therefore, interpret this response in literate adults to be a more domain-general response related to the perception of

motion rather than being related to letter production, specifically.

Processing motion information during letter production may contribute to the general development of the motion sensitive neural responses but only in so far as processing any motion would contribute to their development. There is no indication that bilateral MT/V5 and/or right precuneus participate in letter perception in literate adults (James & Gauthier, 2006; Longcamp et al., 2003) but there is extensive work to suggest that these regions participate in motion perception (Tootell et al., 1995; Zeki et al., 1991; for review see Cavana & Trimble, 2006). We, therefore, interpret the responses found in the younger and older children to be precursors to the adult response associated with the visual processing of motion. This interpretation is in line with the typical developmental trajectory for motion perception ability. The ability to process some forms of motion matures even as early as infancy but motion perception processes as a whole are not fully mature until early adolescence (for review see Hadad, Schwartz, Maurer, & Lewis, 2015). Our whole-brain ANOVA found no differences between groups for the dynamic unfolding contrast, further suggesting that the responses in bilateral temporal cortices and right precuneus in the children were precursors to the literate adult response.

Handwritten forms. We suggest that the variability in form present in handwritten letters may be a particularly important aspect of the visual experience of letter production in young children who are still learning to write and recognize letters. Although much prior work has shown that the fusiform gyrus demonstrates sensitivity to object categories across variations in form, view, and low-level visual features in adults (e.g., Cohen et al., 2002; Dehaene et al., 2001, 2002; Grill-Spector et al., 1999), there is also work that demonstrates some sensitivity to variability within the category itself. The visual word form area (VWFA), for instance, demonstrates a greater response for words presented in a novel format than for words presented in a canonical format (Kronbichler et al., 2009; Wimmer, Ludersdorfer, Richlan, & Kronbichler, 2016). In the case of letter perception, the right fusiform gyrus is more sensitive to handwritten letters, whether they were written by the observer or another person, than to typed letters (Gauthier et al., 2006; Chapter 3). These studies suggest that, at least in the case of 2-dimensional object perception, a sensitivity to form variations in the fusiform gyri exists in addition to the well-documented

sensitivity to object category.

Our results demonstrate that the perception of handwritten letters, whether they were written by oneself or an age-matched control, affects the neural activity in the fusiform gyri more than typed letters during the early stages of letter learning. Only the younger children demonstrated a greater response to handwritten forms than to typed forms in our whole brain contrasts and revealed significantly greater activation to handwritten forms compared to the other two groups. In this same age group, we also found no greater response for letters written by oneself than for letters written by another, suggesting that, in young children, the fusiform gyrus is recruited during the perception of handwritten letters regardless of ownership. We suggest that the perception of variability present in handwritten forms may be a particularly important part of letter production for children who are just learning to write and recognize letters. Letter production may simply be a natural and effective way to present the perceptual system with variable category exemplars, as letter categorization improves similarly whether children learn symbols by letter production or by visually perceiving the symbols presented in variable fonts (Li & James, 2016).

Our interpretation—that the variability inherent in handwritten forms is a part of how the perceptual system refines its activity and, therefore, 'learns' to recognize letters—is supported by the results of our conjunction analysis that revealed that an area in the left fusiform gyrus demonstrated greater activity in the younger children for handwritten forms compared to the older children. Further, our results revealed greater activity in the older children for typed letters compared to the younger children in this same location, suggesting a change in the response of the left fusiform gyrus from being sensitive to variability in an early stage of learning to being sensitive to typed letters in a later stage of learning. These results are in line with prior work that has demonstrated that the left fusiform gyrus responds selectively to typed letters in literate adults (James & Gauthier, 2006; James et al., 2005) and that experience with letter production can influence this response in preliterate children (James, 2010; James & Engelhardt, 2012).

The left fusiform gyrus was not the only region that was more responsive to handwritten forms in the younger children than in the adults, however. The left intraparietal sulcus was also more responsive to

handwritten forms in the younger children than in adults. Unlike the group differences for handwritten forms in the left fusiform gyrus, the group differences for handwritten forms in the left intraparietal sulcus did *not* overlap with those that were found for typed letter perception. Younger children were more sensitive than adults to handwritten forms in the anterior portion of left intraparietal sulcus whereas the opposite trend, that adults were more sensitive than younger children, was observed in the posterior portion for typed letters. The results of the whole brain contrasts (Figure 17) suggest that both of these results were related to the onset of a response to typed letters in the dorsal visual stream in adults. Both anterior and posterior portions of the left intraparietal sulcus demonstrated a significant response to typed letters in adults that was not observed in the younger children. While the response in left anterior intraparietal sulcus was greater for handwritten than typed letters in younger children the responses for handwritten and typed letters in adults were not significantly different from one another. Although it is difficult to interpret based on this study alone, it is possible that the dorsal visual stream responds to form variability at an early age, similar to the ventral visual stream, and begins to respond to letters as a category with experience. This developmental trajectory is, similar to our other results, indicative of an early sensitivity to handwritten forms before sensitivity to letters themselves.

Ownership. Only the posterior portion of the left intraparietal sulcus demonstrated any sensitivity to the perception of one's own handwriting and only in the literate adult group. Prior work in literate adults has found left intraparietal sulcus as well as right posterior fusiform gyrus for letters presented in one's own handwriting compared to typed letters (Chapter 3) but only right posterior fusiform gyrus responded for letters presented in handwritten 'font' compared to typed letters (Gauthier, Wong, Hayward, & Cheung, 2006). Here, we found that the response in left intraparietal sulcus can be attributed to some difference between one's own handwritten forms and another's because we found no difference between another's handwritten forms and typed letters in this parietal region. Our results, in the context of prior work, suggest that the response in the right posterior fusiform gyrus may be related to some perceptual process, the variability present in one's own handwritten forms perhaps, whereas the response in the left intraparietal sulcus may be related to the perception of one's own kinematic cues.

We propose that this parietal response is related to the visual processing of the cues for motion present in handwritten letters (i.e., kinematic cues) and that this response is strongest for one's own handwritten forms because they contain visual cues unique to the observer's own handwriting experiences. The left intraparietal sulcus may be more responsive to one's own handwritten letters than to another's in literate adults because it is responding to visual cues for online modifications of the letter's stored somatomotor plans. Real-time visual cues that point to online changes in the action, such as a curve that went a bit too far to the right while making an "R", may invoke these parietal responses in expert writers who have acquired their own stereotyped movement patterns for each letter as well as a large amount of experience with them. Several recent neurophysiological studies have suggested that the left intraparietal sulcus does, in fact, store some memory of a past experience of visual-motor coordination (Ferrari-Toniolo, Visco-Comandini, Papazachariadis, Caminiti, & Battaglia-Mayer, 2015; Haar et al., 2015; Kastner, Chen, Jeong, & Mruczek, 2017), perhaps accumulating evidence for potential motor movements (Tosoni, Galati, Romani, & Corbetta, 2008), and this same region has been associated with visual-motor coordination during letter production in adults (Haar et al., 2015; Kadmon Harpaz et al., 2014; Chapter 3).

Although our group comparisons yielded no significant differences among groups for the ownership contrast, we must still consider why younger and older children did not also demonstrate sensitivity to one's own handwritten forms. There could be two reasons for this. First, the younger children may not have developed their own stereotypical letterforms and, therefore, are unable to respond to their own kinematic cues in the letterforms. The amount of variability in one's own handwritten forms is very large during the early stages of letter learning and decreases steadily with age before another stage of refinement begins in early adolescence (Hamstra-Bletz & Blöte, 1990; Newland, 1932; Weintraub, Drory-Asayag, Dekel, Jokobovits, & Parush, 2007; Ziviani & Elkins, 1984). This suggests that an individual may not even have their 'own' versions of letters until late adolescence or adulthood. Second, even if they have developed their own stereotypical letterforms, they may not have gained enough experience with them to discriminate their own from another age-matched control. Their visual-motor

guidance systems may not be experienced enough with the visual cues present in their handwritten forms to demonstrate sensitivity to records of movement produced by oneself (kinematic cues in the letter forms) compared with those produced by another age-matched individual. That a certain level of experience is required before being able to discriminate one's own letterforms from another's is an empirical question that has yet to be addressed. Given the subtleness of the differences between one's own handwriting and an age-matched control's, however, discriminating between these two letterforms would understandably take a stable version of one's own letterforms followed by an immense amount of visual experience with them.

Conclusion

We originally hypothesized that letter production contributes to the establishment of a sensorimotor network that supports letter recognition (Chapter 1), in line with sensorimotor theories of neural representation (McClelland et al., 1995; Versace et al., 2009) and several prior works on the development of letter perception that have suggested the same (James, 2010; James & Engelhardt, 2012; James & Kersey, 2013; James, 2017; Longcamp et al., 2003, 2008). We have found, thus far, little evidence for this claim. We suspect that this apparent discrepancy between the current findings and prior works is due to a difference in measurement of brain function. All prior works have measured brain activation during letter perception; they have not measured functional connectivity during letter perception. Although activation and functional connectivity may certainly be related and are often very similar to one another, they are not necessarily the same (Smith et al., 2009; Tomasi & Volkow, 2018; Tomasi, Wang, Wang, & Volkow, 2014).

Compare the results of typed letter perception in literate adults in the current chapter using a measure of neural activation to the results of typed letter perception in literate adults using a measure of functional connectivity (Chapter 4), for example. The current chapter reports a distributed neural response that includes ventral-temporal, parietal, and frontal motor cortices during typed letter perception in literate adults, a finding that has often been interpreted as indication that a sensorimotor network is supporting visual perceptual processes with letters (James & Gauthier, 2006; James & Engelhardt, 2012; Longcamp

et al., 2003, 2008). Chapter 4, however, demonstrates that theses neural systems are not communicating with one another as a part of a sensorimotor network during literate letter perception—their activations are not statistically dependent upon one another above and beyond co-activation due to the task alone. The results of the current chapter suggest, in the context of the results of Chapter 4, that ventral-temporal, parietal, and frontal motor cortices support visual letter perception relatively independent of one another in literate adults.

The ventral-temporal, parietal, and frontal motor responses during visual letter perception were not all apparent in children, however, suggesting that a distributed neural response is not present early in letter learning, but that it develops with experience, as suggested by prior work (James, 2010; James & Engelhardt, 2012). We found that ventral-temporal cortex responds to visually presented letters in literate children (and not early-literate children) and that the response in parietal and frontal motor cortices does not occur until adulthood. We might interpret this to indicate that functional connectivity among these regions during learning 'develops' processes in ventral-temporal cortex faster than processes in motor-oriented dorsal regions. Our other results suggest that this may not be the best interpretation, however. The left fusiform gyrus in ventral-temporal cortex was more sensitive to handwritten than typed forms in preliterate children but was sensitive to the category of letters in early-literate children, suggesting that the visual experiences with letters created by letter production may also contribute to the development of ventral-temporal processes. It suggests that any functional network that might underlie letter production may not be the only mechanism contributing to the development of ventral-temporal perceptual processes.

This interpretation—that ventral-temporal, parietal, and frontal motor regions support letter perception somewhat independently of one another in literate adults and that the responses in each region may have different developmental influences—is in line with the possibility that functional connectivity may be contributing to the development of more localized processes and is not necessarily at odds with the possibility that more localized processes contribute to their own development. By assessing neural responses to the visual perceptual experiences with letters created by letter production, we found that letter sensitivity in ventral-temporal cortex may develop in response to the handwritten forms that are

created during letter production. We note here that, theoretically, visual-perceptual processes can develop based on visual feedback from the motor action alone—they need not develop from neural communication among visual-perceptual, visual-motor, and motor systems. It seems, therefore, that the best interpretation of our findings, in the context of Chapters 2 through 4, is that functional connectivity among regions in the dorsal motor system during letter perception may emerge early on when letter production is essentially a copying task (Tse et al., 2014) and that the output of this visual-somato-motor functional network contributes to the development of visual-perceptual processes in ventral-temporal cortex.

We now turn to addressing two hypotheses generated by the experiment reported in Chapter 2 that demonstrated that letter production practice led to the emergence of a visual-motor functional network during letter perception in preliterate children. I hypothesized that the spatiotemporal consistency among the motor production experience and the visual perceptual experience created during letter production was the reason that letter production resulted in the emergence of visual-motor functional connectivity during letter perception (Chapter 2). We also hypothesized, based on the results of the experiment reported in Chapter 2, that the emergence of visual-motor functional connectivity during letter perception was related to gains in visual recognition. Chapter 6, therefore, measured training-induced changes in functional connectivity and visual recognition after training with novel symbol production in literate adults.

CHAPTER 6:

VISUAL-MOTOR CONTINGENCY DURING SYMBOL PRODUCTION CONTRIBUTES TO THE DEVELOPMENT OF THE NEURAL SYSTEMS SUPPORTING SYMBOL PERCEPTION AND CONCURRENT GAINS IN SYMBOL RECOGNITION

Letter production is a sensorimotor activity that results in greater gains in letter recognition than other activities, such as typing or visual only learning (Longcamp et al, 2005; Zemlock et al., 2018). This dissertation has been concerned with developing a better understanding of the neural mechanisms underlying the effects that letter production has on letter perceptual processes. The hypotheses of this dissertation have been, in brief, that the visual-motor coordination inherent to letter production coordinates neural activity among visual and motor brain systems and establishes a visual-motor functional network that supports letter perception. Chapters 2 through 4 have, thus far, addressed parts of these hypotheses. In Chapters 2 though 5, I have demonstrated that visual-motor functional connectivity supports letter production (Chapters 3 and 4) and that letter production experience leads to the emergence of visual-motor functional connectivity during letter perception in preliterate children (Chapter 2). The current chapter describes a study that provides more direct evidence for these hypotheses by demonstrating that the visual-motor coordination inherent to letter production, and not some other aspect of letter production, is responsible for the emergence of visual-motor functional connectivity during letter perception.

The third hypothesis of this dissertation—that the emergence of visual-motor functional connectivity during letter perception actually supports letter recognition—has been nuanced by the results of the experiments described in Chapters 4 and 5. Chapter 4 reported an experiment that found no evidence of functional connectivity during letter perception in literate adults, suggesting that functional connectivity is not influential in the process of perception itself—at least in individuals who are experts at letter perception. Chapter 5 suggested, in the context of prior work (Li & James, 2016; Stiles et al., 2013), that the development of visual letter processing in ventral-temporal cortex may be driven by the visual experiences of letter production somewhat independently of the development of the neural systems that

support the motor movements required during letter production. These results are problematic for the hypothesis that functional connections among visual and motor brain systems support letter perception because they suggest that visual and motor brain systems develop relatively independently of each other and, ultimately, function relatively independent of each other during letter perception.

I, therefore, propose a modified version of the third hypothesis: visual-motor functional connectivity indirectly supports visual perception by contributing to the development of other neural mechanisms that support visual perception. Visual-motor functional connectivity may not support perceptual processing directly; rather, it may translate to changes in perceptual processing by supporting the development of some other neural mechanism. Functional connectivity may, for instance, contribute to the development of the visual and motor brain systems that it 'connects' (Amit & Brunel, 1995; Freeman, 1995). Functional connections during letter production and subsequent letter perception would, then, support the development of visual and motor brain systems but may not, in themselves, be necessary for letter perceptual processes. Such a developmental progression has been observed in sensorimotor skill learning (Andres et al., 1999; Basset et al., 2015) and would be predicted as the developmental progression for visual perceptual learning based on the results of the experiments reported in Chapters 2 through 5.

Several prior works have demonstrated that experience with letter production leads to gains in letter recognition in preliterate children (Longcamp et al., 2005; Zemlock et al., 2018) and in adults learning novel symbols (Longcamp et al., 2006, 2008), thereby suggesting that the emergence of visual-motor functional connectivity during letter perception in preliterate children (Chapter 2) might support gains in recognition. This study will, therefore, use recognition as a measure of changes in perceptual processing. If visual-motor functional connectivity translates to perceptual development but is not itself supporting perceptual processes, then measures of recognition and functional connectivity may not necessarily follow one another. Functional connectivity should be highest immediately after a learning experience and fade as time passes. Recognition, however, may be highest immediately after learning or may gradually increase over time. In one scenario, functional connectivity and recognition would both be

greatest immediately after training; functional connectivity would decrease over time while recognition would remain relatively elevated. In the other scenario, functional connectivity and recognition would demonstrate an inverse relationship; functional connectivity would decrease over time while recognition increases. In either case, if visual-motor functional connectivity is related to recognition at all, then conditions that lead to the greatest visual-motor functional connectivity should also be the conditions that lead to the greatest gains in visual recognition.

The experiment described in this chapter, therefore, addresses two primary claims: visual-motor coordination inherent to letter production leads to (1) gains in visual letter recognition and (2) the emergence of visual-motor functional connectivity during letter perception. To these aims, twenty literate adults were trained over the course of two weeks on four sets of novel symbols. Training conditions were designed to manipulate the contingency between the motor and visual experiences of a letter that occur during letter production. Each participant received training with a particular set of symbols through one of four conditions: drawing with ink (motor, dynamic visual), drawing without ink (motor, no dynamic visual), watching a handwritten symbol unfold (no motor, dynamic visual), and watching a static handwritten symbol (no motor, no dynamic visual). Participants underwent three task-based fMRI scanning sessions, one pre-training, one post-training, and one after a no-training delay. Training only occurred between the first and second scanning sessions and included four 1-hour training sessions over the course of four days. During fMRI scanning, participants were presented with the symbols that they had learned in the different training scenarios as well as a fifth set of untrained symbols. A symbol recognition test was administered after each training session and after the third scan to assess changes in their ability to visually recognize the practiced symbols.

I expected that (1) symbol recognition would be best for symbols that were learned through draw with ink training and that (2) functional connectivity among visual and motor brain systems would be greater for these symbols compared with symbols learned through other forms of training. My final prediction was related to the time scales of these training-induced increases in functional connectivity and symbol recognition. I expected that (3) the functional connections found immediately after training would

not be present after the one-week no-training delay, but that recognition performance would remain elevated. These results would suggest that the contingency between the motor and visual experiences of a letter during letter production result in greater visual-motor functional connectivity during letter perception and that this temporary increase in functional connectivity may contribute to more long-term changes in the neural mechanisms supporting letter perception but is not, in and of itself, supporting letter perception.

Materials and Methods

Participants

Twenty-two participants were recruited through word of mouth. Two participants did not begin the study due to MRI contraindications, leaving a total of twenty 19-25 year-old adults (10 females). All participants were native English speakers with no experience with logographic languages and had normal or corrected-to-normal vision. All participants were right-handed and screened for history of neurological illness or trauma.

Stimuli

Stimuli included 400 novel symbols (see Figure 20 for examples). Using novel, unfamiliar symbols is a well-documented approach that controls for individual differences in pretraining symbol knowledge (James & Atwood, 2008; Kersey & James, 2013; Longcamp et al., 2006, 2008) and allows for a cleaner manipulation of visual, auditory, and motor experience with those symbols. The training required 40 symbols while the testing and fMRI scanning required an additional 360 symbols that would not be learned. We initially generated 700 novel symbols and then removed symbols that too closely resembled known symbols as well as symbols that were up-down flips, mirror images, or rotations of other symbols. This filtering process resulted in 400 novel, unique symbols that each had four strokes, no circles, and each line connected to at least one other line. Adobe Illustrator was used to create typed versions of these novel symbols. All symbols were in black ink displayed on a white background at the center of the screen.

Only 40 of the 400 novel symbols were used during training. These 40 were selected carefully to ensure that participants would be likely to spontaneously select the desired stroke order and stroke directions during the drawing conditions. To select the 40 symbols on which participants would receive training, we asked four adults to simply copy each symbol one at a time. Typed versions of the 400 symbols were each presented three times in random order for a total of 1200 symbols written by each of the four adults. These sessions were video recorded and three trained research assistants coded the sessions to determine the stroke order that each symbol was drawn and the stroke direction of each of the four strokes. The 40 symbols selected to be training symbols were those symbols for which each participant spontaneously selected the same stroke order and stroke directions on each of the three times they copied the symbol. These requirements increased the likelihood that the stroke order and stroke direction used by the participants during the drawing conditions matched the stroke order and stroke directions presented to the participants in the watching conditions and, therefore, minimized any differences in stroke orders and/or directions between the draw and watch conditions. The other 360 symbols became novel symbols that were used as unlearned symbols for the functional neuroimaging or distractor symbols for the recognition tasks.

Procedure

Participants completed four days of training with no more than one training session per day. Training days were not required to be consecutive, but all four training sessions were required to be completed within the 5-6-day period between the first and second neuroimaging session. Powerpoint was used to present all stimuli during training. Superlab was used to present stimuli and record measurements during the recognition test.

Training. Each participant learned a set of ten novel symbols in each of four training conditions for a within-participants, between-symbols design. The four training conditions were designed to reflect the components of letter production. The Draw With Ink condition included the motor and dynamic visual aspects of letter production; the Draw No Ink condition only included the motor aspect (no visual feedback); the Watch Dynamic condition included only the dynamic visual presentation of the form; the

Watch No Dynamic condition included neither the dynamic visual nor the motor aspects of letter production. Only the Draw With Ink condition resulted in a visual percept of each symbol that was coincident with the actions used to create it. Each participant, therefore, learned a set of ten symbols in the Draw With Ink block, another ten in the Draw No Ink block, another ten in the Watch Dynamic block, and the last ten in the Watch No Dynamic block. Training symbols were randomly assigned to training conditions across participants.

At each training session, participants sat at a desk with a laptop computer in front of him/her and completed four blocks of training, one for each condition. For each training condition block, a PowerPoint slideshow presented each of the ten symbols for that condition one at a time, six times each, in random order. A typed version of the current symbol was displayed at the top and center of each PowerPoint slide. During Draw With Ink training, participants were asked to copy the typed versions of the symbols that were displayed on the screen into a paper booklet with 4.15 x 5.5 inch white sheets using a pen with ink. The Draw No Ink condition was similar to the Draw Ink condition except that the participants wrote the symbols with a pen without ink. During the Watch Dynamic condition, participants placed their hands palm-down on the desk in front of them and were presented with a handwritten version of the symbol unfolding, as if being written, below the typed version of the same symbol. The Watch No Dynamic condition was similar to the Watch Dynamic condition except that the handwritten symbols shown on the screen were static and not dynamically unfolding. The dynamic handwritten symbols were created by a screen recording of an experimenter copying the symbols. The static handwritten symbols were created by taking the final frame of this screen recording that contained the completed handwritten symbol. Only one dynamic and one no-dynamic version were created for each symbol.

Each slide was timed and advanced to the next slide (i.e., symbol) after a certain amount of time had passed. The amount of time allotted for each slide at each training session was experimentally determined to account for practice-induced changes in speed that were observed during piloting and to equate, as much as possible, exposure times between the draw and watch conditions. The time allotted to each symbol in the *draw* conditions was 5.5 – 8.5 seconds with a 7.0 second average. The distribution

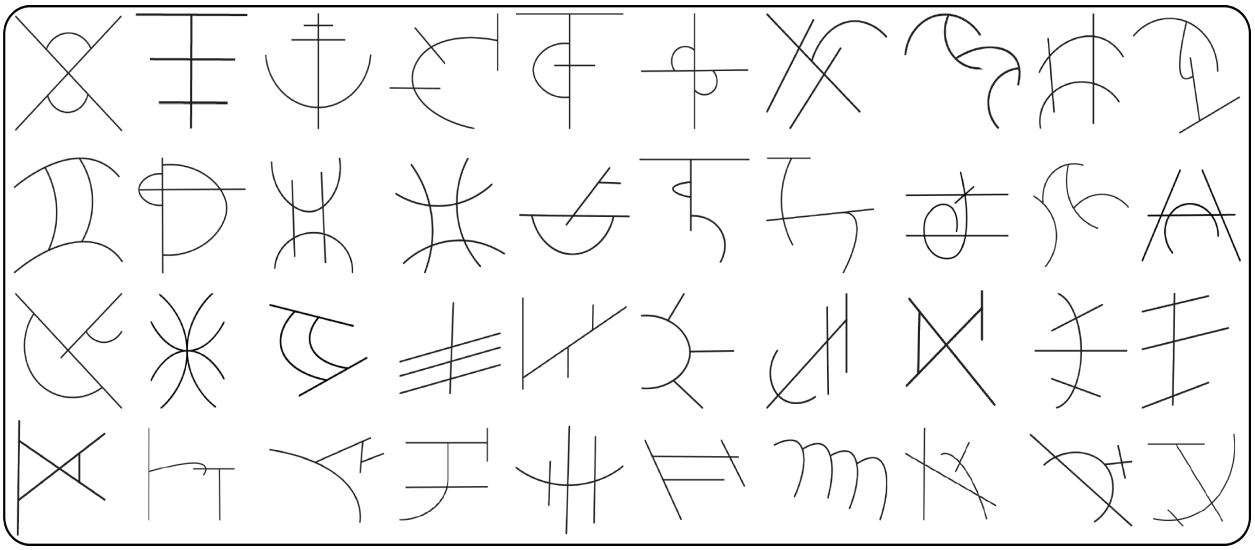

Figure 20. Examples of novel pseudoletters. Four hundred novel, unique symbols were constructed. Each symbol had four strokes, no circles, and each line of the symbol connected to at least one other line of the symbol. Forty of these symbols were selected as targets (symbols on which participants would receive training) and the remaining symbols were used as distractors.

was skewed to the longer times for the first training day and gradually moved to being skewed to the shorter times for the final training day. The time allotted to each symbol in the *watch* conditions was also between 5.5 – 8.5 seconds with a 7.0 second average but the distribution was skewed to the shorter times for all training days. This provided the best match in exposure times between the drawing and watch conditions while accounting for differences in processing times between the motor and visual systems.

Each training block lasted about 10 minutes and the entire training session lasted no more than 45 minutes. The order of training blocks was randomized, within and across participants.

Recognition Testing. Participants were asked to perform an old/new recognition judgement immediately following each training session and at the final scanning session. During recognition testing, participants were presented with static, *typed* versions of the 40 learned symbols along with 40 novel distractors one at a time in random order. Note that the typed forms of the symbols were seen at the top of the screen during all training conditions, equating exposure across conditions. Each symbol was only presented once at each test. For each symbol, they were instructed to answer yes if they had learned the symbol or no if they had not by pressing the 'yes' or 'no' button on a computer keyboard. Half of the participants always pressed yes with their right finger and the other half always pressed yes with their left finger. Before the first recognition task on the first training day, a practice task was administered that consisted of letters and keyboard symbols (e.g., $, &, %) and the participants were asked to press 'yes' for letters and 'no' for symbols. The practice test helped orient participants to the testing context and was repeated until it was clear that they understood the task.

The stimulus presentation time in the recognition test was experimentally determined to ensure that our test was sensitive enough to detect a learning effect from the first to last training days, preferably with a linear slope, and that participants would not reach ceiling too quickly. Each trial began with a 500 ms fixation cross, followed by a 500 ms blank screen, and then a 25 ms stimulus presentation during which a stationary symbol was displayed in the center of the screen. After the stimulus presentation ended, the symbol was replaced by a noise mask until the participant responded. The noise mask was followed by a 500 ms black screen after which a new trial would begin. If the participant responded

before the symbol was replaced by the noise mask, the program advanced to the blank screen for 500 ms before moving on to the next trial. Reaction time and accuracy were measured.

Neuroimaging. Functional neuroimaging was performed before training, after training, and after a no-training delay of approximately one week. Each functional neuroimaging session was required to be within 6-7 days of the previous neuroimaging session. Each scanning session included an anatomical scan followed by a functional localizer run and then three experimental runs. During the localizer and experimental runs, participants performed a one-back identification task in order to keep their attention. A one-back identification task was selected because it was a task that could be performed with no prior experience with the stimuli.

For the localizer runs, there were four block types: letters with thin lines, letters with thick lines, shapes with thin lines, and shapes with thick lines. Each block type was repeated three times over the course of the run, for a total of twelve blocks. Each block consisted of 32 stimuli, one presented in each of the 32 trials within a block. The order of the 32 stimuli within each block was pseudo-randomized to ensure that at least 1 and no more than 3 one-backs occurred in each block. The number of one-back match trials per condition were counterbalanced to ensure that the number of one-back match trials in each block type was held constant. Each trial lasted for 500 ms and there were no gaps between trials, resulting in 16-second blocks. Each block was separated by a 12-second inter-block interval. During the inter-block interval, a fixation cross was presented in the center of the screen. The same fixation cross was presented for 20 seconds before the first block of each run and for 20 seconds following the last block of each run. Each localizer run, therefore, totaled 6:04 minutes.

For the experimental runs, there were five block types: symbols learned through draw with ink, symbols learned through draw without ink, symbols learned through watch dynamic, symbols learned through watch no dynamic, and unlearned symbols. All of these symbols were presented in a typed format. Each block type was repeated three times over the course of each run, for a total of fifteen blocks of symbols. Each block contained 32 symbols, one presented in each of the 32 trials within a block in random order. Each symbol was shown for 500 milliseconds, resulting in 16-second blocks. Each trial

lasted for 500 ms and there were no gaps between trials, resulting in 16-second blocks. Each block was separated by a 12-second inter-block interval. During the inter-block interval, a fixation cross was presented in the center of the screen. The same fixation cross was presented for 20 seconds before the first block of each run and for 20 seconds following the last block of each run. Each experimental run, therefore, totaled 7:28 minutes.

Neuroimaging parameters. Neuroimaging was performed using a Siemens Prisma Fit 3-T whole-body MRI system housed in the Indiana University Imaging Research Facility. High-resolution T1-weighted anatomical volumes were acquired using a Turbo-flash 3-D sequence: TI = 900 ms, TE = 2.98 ms, TR = 2300 ms, flip angle = 9°, with 176 sagittal slices of 1.0 mm thickness, a field of view of 256 x 248 mm, producing an isometric voxel size of 1.0 mm^3. For functional images, the field of view was 220 x 220 mm, with an in-plane resolution of 110 x 110 pixels, and 72 axial slices of 2.0 mm thickness per volume with 0% slice gap, producing an isometric voxel size of 2.0 mm^3. Functional images were acquired using a gradient echo EPI sequence with interleaved slice order: TE = 30 ms, TR = 1000 ms, flip angle = 52° for blood-oxygen-level-dependent (BOLD) imaging.

Neuroimaging Preprocessing. All preprocessing steps were performed in BrainVoyager 20.6. Individual anatomical volumes were normalized to Talairach space (Talairach & Tournoux, 1988). Preprocessing of functional data included slice scan time correction, 3-D motion correction using trilinear/sinc interpolation, and 3D Gaussian spatial blurring with a full-width-at-half-maximum of 6 mm. Temporal high-pass filtering was performed using a voxel-wise GLM with predictors that included a Fourier basis set with a cut-off value of 2 sine/cosine pairs and a linear trend predictor. During normalization, functional data were re-sampled to 2 mm^3 isometric voxels. Coregistration of functional volumes to anatomical volumes was performed using a rigid body transformation. All within-session functional runs were aligned to the first functional run within that session. The first functional runs of each session were then coregistered to the anatomical scan acquired in session one.

Neuroimaging Functional Connectivity Analysis.

Parcellation. Two-hundred and sixty-four regions of interest (ROIs) were selected based on a parcellation scheme constructed from a meta-analysis of task-based fMRI as well as a network-based community detection procedure using resting state functional connectivity analysis (Dosenbach et al., 2010; Power et al., 2011). Subcortical ROIs were excluded. The center x-, y-, z-coordinates for each of the 264 ROIs were dilated so that they included 2 voxels on either side of the center voxel. Each ROI, therefore, included one-hundred and twenty-five 2-mm voxels, or a volume of 1000 mm^3 surrounding the center x-, y-, z-coordinate. Preprocessed functional time courses were extracted from all voxels for each run. Average time courses for each ROI were created by averaging across voxels within the ROI.

Community Detection. Each of the 264 ROIs were assigned to mutually-exclusive communities based on the assignments presented in Power et al. (2011) and their correlations with one another during the localizer runs. While the ROIs presented in Power et al. (2011) were selected based on resting-state functional connectivity and task-based fMRI, the partitioning of those ROIs into communities was accomplished by applying a community detection algorithm to only the resting-state data. Resting-state functional connectivity has been shown to be highly modular, with accepted neural systems (e.g., visual, auditory) demonstrating greater within- than between-system connectivity (Cole & Schneider, 2007; Fair et al., 2007; Fox, Snyder, Vincent, & Raichle, 2006; Greicius, Krasnow, Reiss, & Menon 2003). Community detection algorithms on task-based fMRI data result in similar partitions but with some differences in the ROIs assigned to each community (Dwyer et al., 2014; Hearne, Cocchi, Zalesky, & Mattingley, 2017). We, therefore, began with the partition presented in Power et al. (2011) and applied a community detection process to optimize the partition for our data and our task (i.e., letter perception).

We used the Generalized Louvain search algorithm to find the partition with the maximum modularity (Blondel, Guillaume, Lambiotte, & Lefebvre, 2008; Jeub, Bazzi, Jutla, & Mucha, 2017). The Generalized Louvain algorithm uses only the modularity matrix, B, and attempts to maximize modularity by moving ROIs between communities in such a way that increases the quality, Q, of the partition. The

modularity matrix, B, has the same dimensions as the correlation matrix, R, from which it is was created with each entry in B defined by

$$B_{ij} = \sum_{\substack{i=1 \\ j=1}}^{r} (R_{ij} - \gamma N_{ij})$$

where R_{ij} is the observed correlation for ROIs i and j, N_{ij} is the correlation that would be expected under the null hypothesis, γ is a user-defined parameter, and r is the number of ROIs. The degree to which a particular partition achieves the goal of maximal modularity is quantified by the quality function, Q, defined by

$$Q = \sum_{k=1}^{c} B_k$$

where B_k is the modularity for community k calculated by averaging all B_{ij} in community k and c is the number of communities in the partition. The search algorithm evaluates if moving any ROI to another community would increase the overall modularity of the partition, quantified by Q. The move that would result in the greatest increase in Q is performed and another iteration begins. This procedure continues until no movements can create a larger, more positive Q.

A group-averaged partial correlation matrix was constructed by taking the element-wise average of all participants' correlation matrices for the localizer runs, controlling for motion parameters. The null model for correlation matrices is a model in which all pairs of ROIs are equally correlated—all N_{ij} equal one. Gamma, therefore, sets the threshold for modularity values in B that can contribute to making the partition's Q value big and positive.

Communities were detected in two steps. The first step involved selecting the resolution parameter, gamma. The second step involved determining which nodes would be assigned to each network. These two procedures are described in turn.

Defining gamma. Community detection is an iterative procedure and the same gamma may return different communities each time community detection is performed. The γ that is most appropriate for the

data is the γ that produces the most similar communities from one iteration to the next. We tested 20 different values of γ linearly spaced between 0 and 1. For each γ, we generated 1000 community partitions and measured similarity with a normalized pair-counting algorithm, specifically the z-score of the Rand coefficient (Traud, Kelsic, Mucha, & Porter, 2011). Pair counting algorithms compare two partitions at a time by counting the number of times a particular node pair is classified together in both partitions (ω_{11}), in the first but not the second partition (ω_{10}), in the second but not the first partition (ω_{01}), and in neither partition (ω_{00}). The Rand coefficient, S_R, was calculated from these values with the equation

$$S_R = \frac{\omega_{11} + \omega_{00}}{M}$$

where $M = \omega_{11} + \omega_{10} + \omega_{01} + \omega_{00}$. When $S_R = 0$, none of the 1000 partitions generated for that particular γ resulted in similar partitions. When $S_R = 1$, all of the 1000 partitions generated for that particular γ resulted in similar partitions. S_R identifies how similar partitions are, but it is unable to determine if that similarity would be expected by chance (Traud et al., 2011). S_R was, therefore, normalized based on the equation

$$z_{S_R} = \frac{1}{\sigma_{\omega_{11}}}\left(\omega_{11} - \frac{M_1 + M_2}{M}\right)$$

where $M_1 = \omega_{11} + \omega_{10} + \omega_{01} + \omega_{00}$ for the first partition and $M_2 = \omega_{11} + \omega_{10} + \omega_{01} + \omega_{00}$ for the second partition (Traud et al., 2011). We selected the γ that produced the global maximum similarity score, as defined by z_{S_R}, because that is the γ that we would be most likely to find if we were to perform this procedure several more times.

Creating consensus partitions. A partition is a particular assignment of ROIs to communities and a consensus partition is a partition that best represents a set of partitions. To construct a consensus partition, we constructed an agreement matrix for the 1000 partitions produced at our selected γ value. Each element in an agreement matrix indicates the number of times that a particular node pair was assigned to the same community across the 1000 iterations. We then performed an iterative clustering procedure on the agreement matrix using the Generalized Louvain algorithm (as described above) to find

the consensus partition. The clustering procedure looped over all ROI assignments in each partition and determined if moving any particular ROI to a different community would produce a higher quality partition, where quality is quantified by *Q* (Lancichinetti & Fortunato, 2012). This procedure continued until ROI assignments in each of the 1000 partitions converged upon the same partition. The partition onto which the algorithm converged was taken as a consensus partition, the best representation of the 1000 partitions, because it is the partition closest (i.e., the least number of nodes moved) to each of the 1000 original partitions.

Functional Connectivity Analysis. Our first step was to determine if any functional connections were related to visual-motor training that resulted in the production of a temporally coincident visual percept. We, therefore, evaluated the change in the functional connectivity associated with the interaction between the MOTOR and VISUAL factors between sessions, akin to evaluating the significance of a three-way interaction between MOTOR, VISUAL, and SESSION with a measurement of functional connectivity as the dependent measure. We used beta-weights from a psychophysiological interactions (PPI) analysis on the data collected during the experimental runs at each session as our measurement of functional connectivity (Friston et al., 1999; O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012). Each community identified by our community detection algorithm was treated as a seed for PPI.

For each community and at each session, we constructed a PPI model that included a *psychological predictor* for the interaction between MOTOR and VISUAL factors (i.e., (DI>DnI)>(WD>WnD)), a *physiological predictor* representing the activity of the seed community, and a *psychophysiological* predictor representing the interaction between the *psychological* and *physiological* predictors, and a set of nuisance predictors. The *psychological* predictor was constructed by convolving the dummy-coded task predictor for the DI, DnI, WD, and WnD conditions with a single-gamma hemodynamic response function (Boynton, Engel, Glover, & Heeger, 1996) and then combining these predictors to produce a single psychological predictor representing the interaction between MOTOR and VISUAL factors (i.e., (DI>DnI)>(WD>WnD)). The *physiological* predictor was constructed by averaging the activation time course across all ROIs within the community. The *psychophysiological* predictor was

constructed by an element-wise multiplication between the psychological and physiological predictors. The nuisance predictors included rigid body motion regressors (Bullmore et al., 1999) and spike regressors for each time point at which the relative root mean squared (RMS) time course exceeded 0.5 mm (Satterthwaite et al., 2013). All independent and dependent variables were standardized.

Between-session differences were evaluated for significance by subtracting the beta-weights between two sessions of interest (e.g., Sessions 1 and 2) for each subject and comparing the distribution of the resulting values with a null distribution. The null distribution was constructed from 10,000 random selections where each selection was the difference between beta-weights for two sessions of interest from one of all possible permutations of the order of session. For each random selection, the pairing between the permutation selected and the subject selected was also allowed to vary randomly, thereby treating subjects as random effects. The null distribution was then estimated at the group-level and compared to the real distribution at the group-level to determine the likelihood of finding the real distribution by chance. The distance between the real distribution and the null distribution was quantified by a z-score for each community pair. Z-scores were considered significant if they passed a $p < .05$ threshold after an FDR adjustment based on the linear step up procedure with $q < .10$ (Benjamini & Hochberg, 1995).

Communities that underwent significant changes in functional connectivity between sessions were further evaluated by assessing the strength of the interaction between MOTOR and VISUAL factors at each level of SESSION, akin to evaluating the simple interaction effects after finding a significant three-way interaction. Similar to the between-session assessment, a null distribution was constructed from 10,000 random selections where each selection was the beta-weight associated with the interaction between MOTOR and VISUAL from one of all possible permutations of the order of condition in the interaction contrast (i.e., (DI>DnI)>(WD>WnD), (DnI>WD)>(WnD>DI), etc.). As with the between-session assessment, subjects were treated as random effects and the distance between the null and real distributions at the group level was subjected to the same significance criteria.

Communities that demonstrated a significant simple interaction effect at any one session were further evaluated by extracting the standardized beta-weights at each session from a generalized PPI

model (McLaren et al., 2012; O'Rielly et al., 2012). A generalized PPI (gPPI) model was used for this comparison to evaluate functional connectivity associated with each condition because extracting condition-specific beta-weights is impossible with the standard PPI method when an interaction is tested. All conditions in an interaction must be combined into one psychophysiological predictor in the standard PPI method leaving no condition-specific beta-weights to be extracted. The gPPI model included four *psychological* predictors, one for each condition of interest: DI, DnI, WD, and WnD. Each of these predictors was constructed by convolving the dummy-coded task predictor for each condition with a single-gamma hemodynamic response function (Boynton et al., 1996). The *physiological* predictor was, again, the average activation time course across all ROIs within the community. The *psychophysiological* predictors were constructed by an element-wise multiplication of each psychological predictor with the physiological predictor, result in four psychophysiological predictors—one for each condition. The nuisance regressors used in the standard PPI model were also included in this model as predictors of no interest. All independent and dependent variables were standardized.

I then performed a series of ANOVA-based comparisons on the gPPI beta-weights for each significant community pair. We first verified that the same three-way interaction and simple interaction effects with the sPPI model and permutation tests were also found with the gPPI model and a standard ANOVA, given that gPPI has less power than sPPI (McLaren et al., 2012; O'Rielly et al., 2012). Simple interaction effects were only evaluated at each level of SESSION because these effects at each level of MOTOR and VISUAL were of no interest. Factors included MOTOR, VISUAL, and SESSION. MOTOR had 2 levels: draw, watch. VISUAL had 2 levels: dynamic visual, no dynamic visual. SESSION had 3 levels: session 1, session 2, and session 3. Significant simple interaction effects at any level of SESSION were followed with planned paired t-tests: DI vs. DnI, DI vs. WD, and DI vs. WnD.

Results

Recognition Testing

Data points were considered outliers if they fell above or below 3 standard deviations of the within-condition, within-day mean and were removed. An additional two trials were omitted because the reaction time measure indicated that they had responded prematurely.

We performed two Three-way Repeated-measures ANOVAs, one for accuracy and one for reaction time. For both models, MOTOR, VISUAL, and DAY were entered as a within-participant factors. MOTOR had two levels, corresponding to the manipulation of the motor experience (Draw, Watch) and VISUAL had two levels, corresponding to the manipulation of the visual experience with the symbol (Dynamic, No Dynamic). DAY had three levels (Day 1, Day 4, Day 5), corresponding to the training days immediately after the first training day (Day 1), after the training week (Day 4), and after the no-training delay (Day 5). The ANOVA with reaction time was calculated using only correct trials. Each omnibus ANOVA was followed by planned comparisons for DAY. Planned comparisons for DAY were one-tailed paired t-tests between Days 1 and 4, between Days 4 and 5, and between Days 1 and 5. We also calculated dprime and performed the same statistical procedures. Results were the same as accuracy and I, therefore, only report on accuracy.

Reaction time. Mauchly's test indicated a violation of sphericity for DAY, χ^2 (2) = 25.593, p = .000, for the MOTOR*DAY interaction, χ^2 (2) = 10.504, p = .005, for the VISUAL*DAY interaction, χ^2 (2) = 17.560, p = .000, and for the three-way interaction, χ^2 (2) = 22.217, p = .000. The Greenhouse-Geisser Epsilon values for all sphericity violations were less than 0.75. We, therefore, applied the Greenhouse-Geisser correction for DAY, MOTOR*DAY, VISUAL*DAY, and the three-way interaction. The three-way repeated-measures ANOVA for reaction time revealed main effects of MOTOR, F(1, 19) = 8.530, p = .009, VISUAL, F(1, 19) = 13.186, p = .002, and DAY, F(1.137, 21.607) = 47.840, p = .000. The analysis also revealed a significant two-way interaction between MOTOR and VISUAL, F(1, 19) = 9.402, p = .006. The interactions between DAY and MOTOR and between DAY and VISUAL were not

significant, $F(1.387, 26.351) = 2.438$, $p = .121$, and, $F(1.232, 23.413) = 1.346$, $p = .272$, respectively. The three-way interaction was not significant, $F(1.170, 22.236) = 3.389$, $p = .074$.

Post hoc comparisons for MOTOR*VISUAL revealed that participants responded faster when presented with symbols learned through Draw Ink ($M = 716.77$, $SE = 15.382$) than symbols learned through Draw No Ink ($M = 804.000$, $SE = 26.837$), $p = .000$, Watch Dynamic ($M = 794.099$, $SE = 22.612$), $p = .000$, and Watch No Dynamic ($M = 792.381$, $SE = 19.852$), $p = .000$, all Bonferonni corrected. There were no differences between Draw No Ink and Watch Dynamic, $p = .58$, between Draw No Ink and Watch No Dynamic, $p = .59$, and Watch Dynamic and Watch No Dynamic, $p = .919$ (Figure 21).

Planned comparisons for DAY revealed that participants responded faster on day 4 ($M = 691.571$, $SE = 16.250$) compared to day 1($M = 934.607$, $SE = 34.563$), $p = .000$, and on day 5 ($M = 704.265$, $SE = 19.074$) compared to day 1, $p = .000$. There was no difference between reaction time on day 4 compared to day 5, $p = .116$ (Figure 22).

Accuracy. Mauchly's test indicated a violation of sphericity for the MOTOR*DAY interaction, $\chi^2 (2) = 6.186$, $p = .045$, and the VISUAL*DAY, $\chi^2 (2) = 0.681$, $p = .003$. The Greenhouse-Geisser Epsilon values for both were less than 0.75. We, therefore, applied the Greenhouse-Geisser correction for MOTOR*DAY and VISUAL*DAY. The two-way repeated-measures ANOVA for accuracy revealed a main effects of DAY, $F(2, 38) = 6.008$, $p = .005$, MOTOR, $F(1, 19) = 8.687$, $p = .008$, and VISUAL, $F(1, 19) = 10.880$, $p = .004$. Participants were more accurate in the drawing conditions ($M = .905$, $SE = .010$) compared to the watching conditions ($M = .814$, $SE = .032$) and in the dynamic visual conditions ($M = .882$, $SE = .017$) compared to the conditions with no dynamic visual ($M = .837$, $SE = .022$). The DAY*MOTOR interaction was not significant, $F(2, 38) = 0.917$, $p = .408$, and neither were the DAY*VISUAL and MOTOR* VISUAL interactions, $F(2, 38) = 0.014$, $p = .997$, and, $F(1, 19) = 0.318$, $p = .579$, respectively. The three-way interaction was not significant, $F(2, 38) = .005$, $p = .756$.

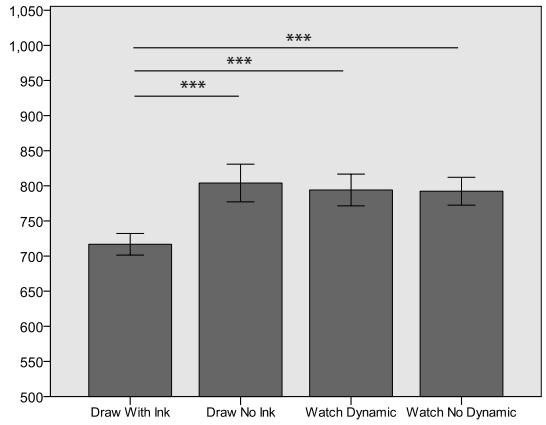

Figure 21. Fastest Reaction Times for Symbols Learned in Draw With Ink. A Three-way repeated-measures ANOVA for reaction time revealed a significant two-way interaction between MOTOR and VISUAL, $F(1, 19) = 9.402$, $p = .006$. Participants responded faster when presented with symbols learned through Draw Ink ($M = 716.77$, $SE = 15.382$) than symbols learned through Draw No Ink ($M = 804.000$, $SE = 26.837$), $p = .000$, Watch Dynamic ($M = 794.099$, $SE = 22.612$), $p = .000$, and Watch No Dynamic ($M = 792.381$, $SE = 19.852$), $p = .000$, all Bonferroni corrected. There were no differences between Draw No Ink and Watch Dynamic, $p = .58$, no differences between Draw No Ink and Watch No Dynamic, $p = .59$, and no differences between Watch Dynamic and Watch No Dynamic, $p = .919$. *** $p < .001$.

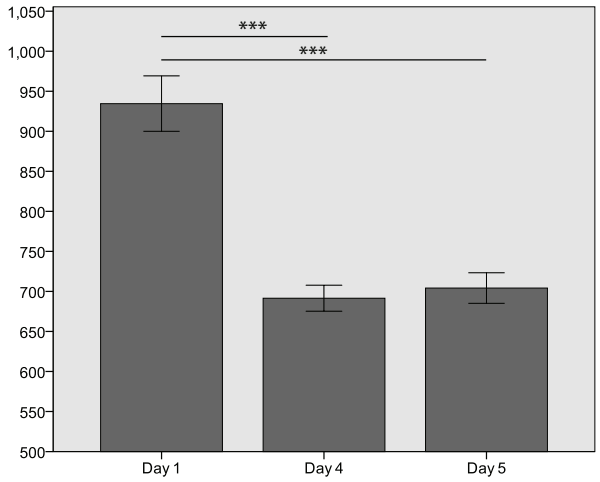

Figure 11. Faster Reaction Times After Training than Before Training. Participants responded faster after the last day of training (day 4: *M* =691.571, *SE* = 16.250) and after a week-long no-training delay (day 5: *M* = 704.265, *SE* = 19.074), compared to the first day of training (day 1: *M* = 934.607, *SE* = 34.563), both *ps* = .000. *** $p < .001$.

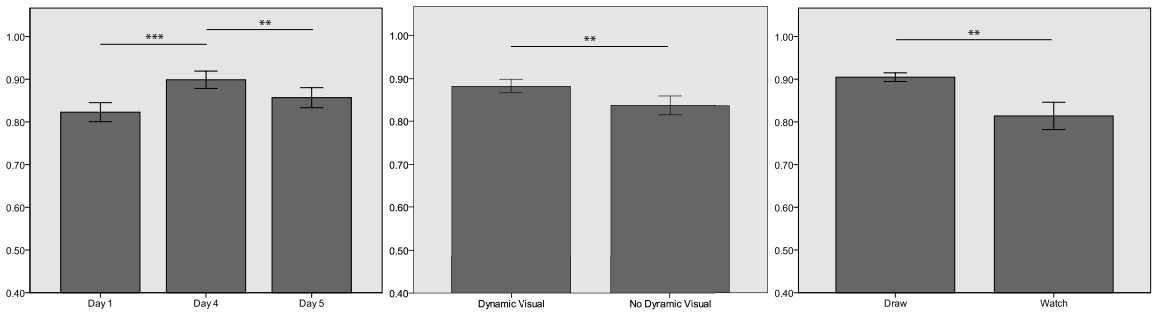

Figure 23. Main Effects of Day, Motor, and Visual for Accuracy. A Two-way repeated-measures ANOVA for accuracy revealed main effects of DAY, $F(2, 38) = 6.008$, $p = .005$, MOTOR, $F(1, 19) = 8.687$, $p = .008$, and VISUAL, $F(1, 19) = 10.880$, $p = .004$. Participants were more accurate in the drawing conditions ($M = .905$, $SE = .010$) compared to the watching conditions ($M = .814$, $SE = .032$) and in the dynamic visual conditions ($M = .882$, $SE = .017$) compared to the conditions with no dynamic visual ($M = .837$, $SE = .022$). Planned comparisons for DAY revealed that participants were more accurate after four days of training (day 4: $M = .899$, $SE = .020$) compared than on their first day of training (day 1: $M = .823$, $SE = .022$), $p = .001$, and compared to after a week-long no-training delay (day 5: $M = .857$, $SE = .023$), $p = .01$. There was no difference in accuracy between their first day of training and after the no-training delay, $p = .203$. *** $p < .001$, ** $p < .01$.

Planned comparisons for DAY revealed that participants were more accurate on day 4 (M = .899, SE = .020) compared to day 1(M = .823, SE = .022), p = .001, and compared to day 5 (M = .857, SE = .023), p = .01. There was no difference between day 1 and day 5, p = .203 (Figure 23).

Neuroimaging

Parcellation and community detection. The gamma-detection procedure suggested two γ values, 0.4211 and 0.8421, with z_{S_R} values of 108 and 163, respectively. We, therefore, selected a γ of 0.8421. This γ produced a consensus partition that included 13 communities with a Q value of 5.61 x 10^6. The correlation matrix for the consensus partition is displayed in Figure 24 along with the agreement matrix across the 1000 iterations produced at γ = 0.8421. Most communities demonstrated a very high agreement among iterations, with the exception of community 12 and, to a lesser extent, with the exception of community 4. Whereas there was near perfect agreement between iterations for most communities, some of the ROIs that were assigned to communities 12 and 4 in the consensus partition were assigned to other communities in some iterations. In partitions where ROIs from communities 12 and 4 were not assigned to those communities, they were most often assigned to community 6 and, to a lesser extent, to communities 2, 3, and 7. Community 2 had two ROIs that were, in some partitions, assigned to community 1.

The division of ROIs into the communities presented in Power et al. (2011) was, in general, retained after the community detection procedure. Exceptions were associated with the communities from the optimized partition that displayed the least agreement across iterations, communities 1 and 2 as well as communities 3, 4, 6, 7, 8, and 12. Figure 25 displays the relationship between the original partition presented in Power et al. (2011) and the optimized partition used here. Appendix C lists the Talairach X-, Y-, and Z-coordinates for the optimized partition as well as the community to which that ROI was assigned in the original Power et al. (2011) partition.

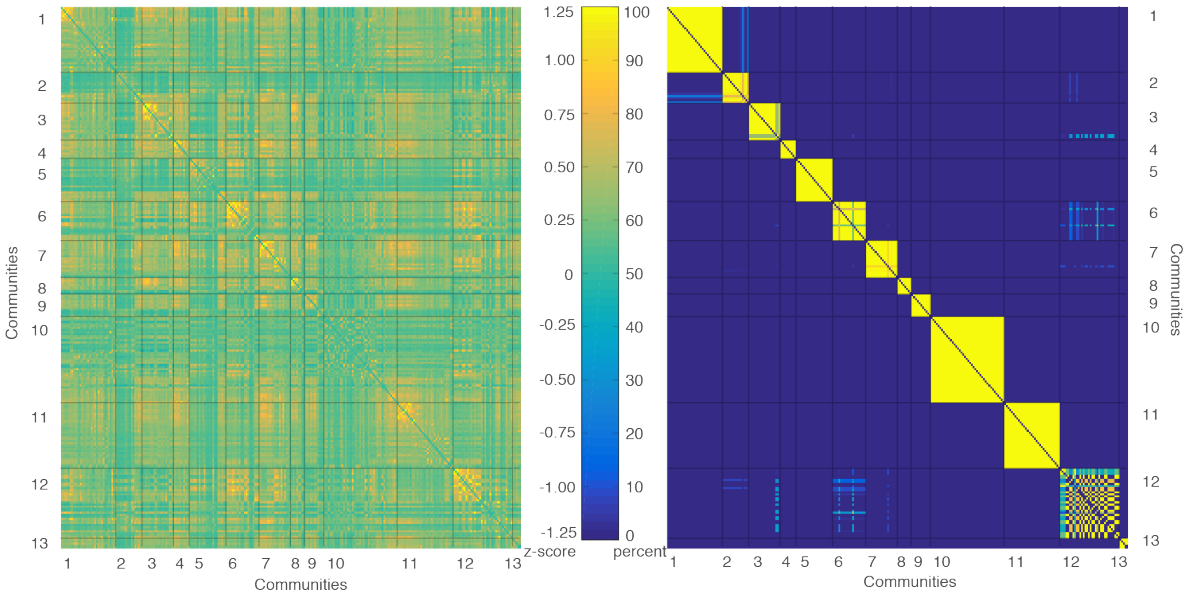

Figure 24. Consensus Partition. Correlation matrix for the consensus partition (left) and agreement matrix (right) for all iterations with $\gamma = 0.8421$. The correlations are presented as a z-score, calculated from the correlation matrix with a Fisher's r-to-z transformation. The agreements are presented as a percentage, calculated as the percent of the total 1000 iterations in which a particular ROI was assigned to the same community to which it was assigned in the consensus partition. Most communities demonstrated near perfect agreement across all iterations. Communities 12 and 4 demonstrated less perfect agreement and were most often assigned to community 6 when they were not assigned to 12 or 4, respectively.

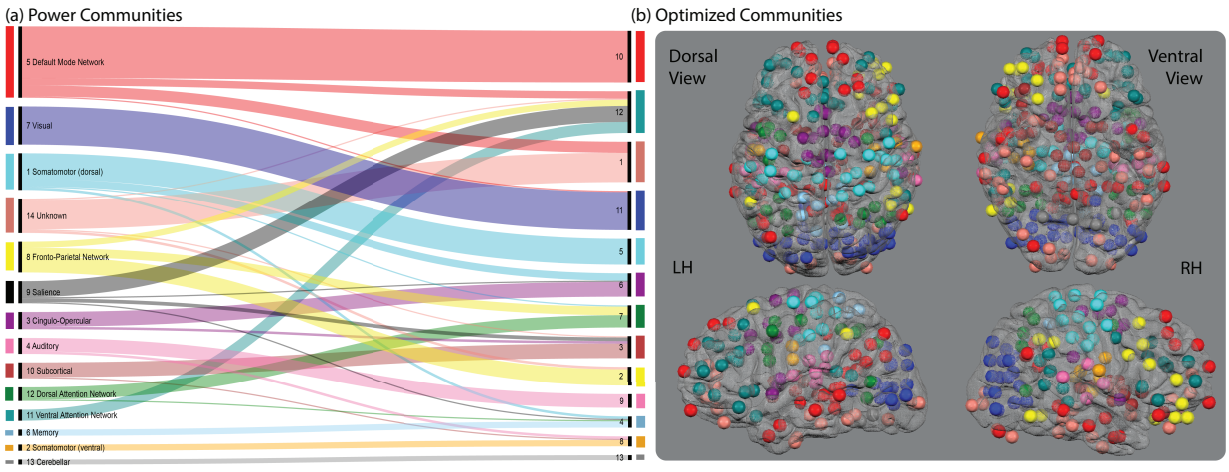

Figure 25. Relationship Between Power Communities and Optimized Communities. (a) A large portion of the original communities presented in Power et al. (2011) were retained after optimizing the partition for our data set and task. The most notable exceptions included the optimized communities 4 and 12 that were constructed of ROIs from several different communities in the Power et al. (2011) partition. The alluvial flow chart was produced using RAWGraphics Software at rawgraphs.io (Mauri, Elli, Caviglia, Uboldi, & Azzi, 2017). **(b)** The 264 ROIs are displayed on a glass brain and color coded for their community assignment in the optimized community. ROI sizes were reduced for display. The actual ROI radii were about twice as large as those displayed here.

Functional connectivity analysis. All communities demonstrated a three-way interaction with at least one other community besides community 12. Community pairs that demonstrated a significant three-way interaction effect were separable into two, non-overlapping clusters of community pairs. The first cluster included communities 2, 3, 6, 8, 9, 11, and 13. The second cluster included communities 1, 4, 5, 7, and 10. Matrices displaying the z-scores of significant community pairs are presented in Figure 26.

All ANOVA-based analyses with the gPPI-estimated beta-weights were consistent with the results of the permutation tests using the sPPI-estimated beta-weights. We, therefore, report on only the results of the permutation tests using sPPI-estimated beta-weights below as well as the planned paired t-tests using the gPPI-estimated beta-weights. Results are provided for each cluster separately.

Cluster 1: Communities 2, 3, 6, 8, 9, 11, and 13. There were no significant functional connections associated with the VISUAL*MOTOR interaction before training at Session 1 or after the no-training delay at Session 3. There were, however, six community pairs that demonstrated a significant VISUAL*MOTOR interaction immediately after training at Session 2 in this cluster (Figure 27). The backbone of this cluster included communities 8, 9, and 11. Each of these communities were directly relatable to original communities reported in Power et al. (2011): Somatomotor (Ventral), Auditory, and Visual.

The periphery of this cluster included communities 2, 3, 6, and 13. Community 2 was comprised of a subset of the Fronto-Parietal community reported in Power et al. (2011). Community 3 was largely comprised of the Subcortical community originally reported in Power et al. (2011) with a few additional ROIs. Community 6 was comprised of two communities from the Power et al. (2011) parcellation: a subset of the Somatomotor (Dorsal) community and the entire Cingulo-Opercular community. Community 13 was exactly the same as the original Cerebellar community reported in Power et al. (2011).

Communities 2 and 9. Planned paired t-tests indicated that functional connectivity between communities 2 and 9 at Session 2 was marginally greater for DI (M = .016, SE = .046) than for DnI (M = -.079, SE = .043), $t(19) = 1.723$, $p = .100$. There was no difference between DI and WD (M = -.027, SE =

.036), $t(19) = .808$, $p = .429$, or between DI and WnD ($M = .057$, $SE = .040$), $t(19) = 0.694$, $p = .496$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Communities 3 and 11. Planned paired t-tests indicated that functional connectivity between communities 3 and 11 at Session 2 was greater for DI ($M = .022$, $SE = .038$) than for DnI ($M = -.079$, $SE = .046$), $t(19) = 2.593$, $p = .018$. There was no difference between DI and WD ($M = -.070$, $SE = .041$), $t(19) = 1.442$, $p = .165$, or between DI and WnD ($M = .041$, $SE = .041$), $t(19) = 0.386$, $p = .704$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Communities 6 and 9. Planned paired t-tests indicated that functional connectivity between communities 6 and 9 at Session 2 was no different for DI ($M = -.007$, $SE = .044$) compared to DnI ($M = -.073$, $SE = .049$), $t(19) = 1.260$, $p = .223$, compared to WD ($M = -.038$, $SE = .037$), $t(19) = 0.685$, $p = .501$, or compared to WnD ($M = .016$, $SE = .046$), $t(19) = 0.447$, $p = .660$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Communities 8 and 11. Planned paired t-tests indicated that functional connectivity between communities 8 and 11 at Session 2 was greater for DI ($M = .049$, $SE = .041$) than for DnI ($M = -.059$, $SE = .050$), $t(19) = 1.944$, $p = .067$. DI was marginally larger than WD ($M = -.050$, $SE = .043$), $t(19) = 1.71$, $p = .110$, but there was no difference between DI and WnD ($M = -.56$, $SE = .039$), $t(19) = 0.135$, $p = .894$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Communities 8 and 13. Planned paired t-tests indicated that functional connectivity between communities 8 and 13 at Session 2 was greater for DI ($M = .050$, $SE = .039$) compared to DnI ($M = -.078$, $SE = .043$), $t(19) = 2.584$, $p = .018$. There was no difference between DI and compared to WD ($M = -.007$, $SE = .049$), $t(19) = .848$, $p = .407$, or between DI and WnD ($M = .057$, $SE = .041$), $t(19) = 0.124$, p

= .902. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Communities 9 and 11. Planned paired t-tests indicated that functional connectivity between communities 9 and 11 at Session 2 was greater for DI (M = .006, SE = .042) compared to DnI (M = -.140, SE = .043), $t(19) = 2.793$, $p = .012$. DI was marginally greater than WD (M = -.098, SE = .031), $t(19) = 1.930$, $p = .069$. There was no differences between DI and WnD (M = .013, SE = .035), $t(19) = 0.170$, $p = .867$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

Cluster 2. There were no significant functional connections associated with the VISUAL*MOTOR interaction before training at Session 1 or after the no-training delay at Session 3. There was only one community pair that demonstrated a significant VISUAL*MOTOR interaction immediately after training in this cluster at Session 2: communities 1 and 7 (Figure 28). Community 1 was comprised of the Unknown Power et al. (2011) community and a subset of ROIs from the Default Mode Network Power et al. (2011) community. Community 7 was comprised of the entire Dorsal Attention Network Power et al. (2011) community as well as a subset of ROIs from the Fronto-Parietal Network Power et al. (2011) community.

Planned paired t-tests indicated that functional connectivity between communities 1 and 7 at Session 2 was no different for DI (M = -.007, SE = .049) compared to DnI (M = -.078, SE = .037), $t(19) = 1.409$, $p = .175$, compared to WD (M = -.058, SE = .042), $t(19) = .898$, $p = .380$, or compared to WnD (M = .024, SE = .031), $t(19) = 0.631$, $p = .536$. We also performed exploratory post hoc paired t-tests for Session 3 and found no significant differences between any two conditions.

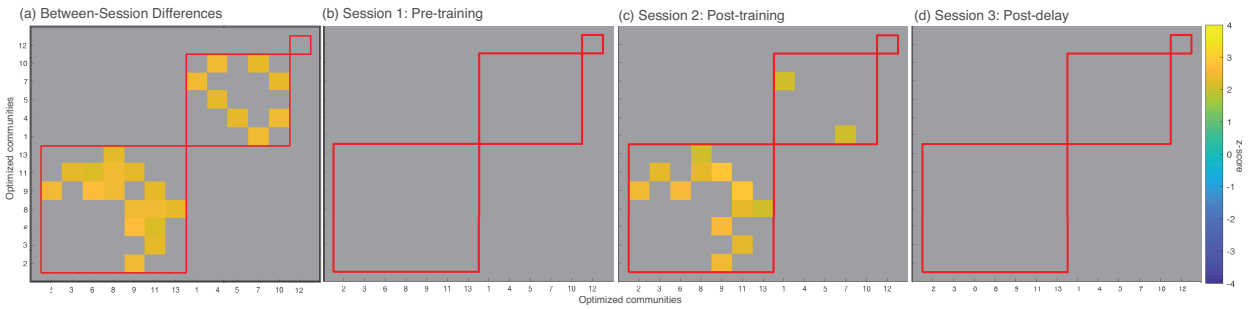

Figure 26. Significant Differences in Functional Connectivity Between Sessions. Each matrix displays z-scores for community pairs that demonstrated significant changes in functional connectivity among sessions. All between-session differences were between Session 2 and Session 3. There were no differences between Sessions 1 and 2 or between Sessions 1 and 3. Communities pairs are organized into three non-overlapping clusters based on their between-session changes in connectivity. Red lines mark the boundaries of the three community clusters. All communities demonstrated some change in connectivity, except for community 12. **(a)** The overall three-way comparison indicated that functional connectivity associated with the interaction between motor and visual factors was significantly different between sessions in two non-overlapping community clusters. The first of these community clusters included communities 2, 3, 6, 8, 9, 11, and 13 with the majority of this cluster's connections being associated with community 11. The second of these community clusters included communities 1, 4, 5, 7, and 10. **(b)** Community pairs that demonstrated a significant three-way interaction were evaluated for simple interaction effects between MOTOR (draw, watch) and VISUAL (dynamic visual, no dynamic visual) at each level of SESSION (pre-training, post-training, post-delay). There were no community pairs that demonstrated a significant simple interaction between MOTOR and VISUAL factors before training at Session 1. **(c)** Several community pairs demonstrated a significant simple interaction between MOTOR and VISUAL factors after training at Session 2. For the first community cluster, these community pairs include 2 – 9, 6 – 9 , 3 – 11, 8 – 11, 9 – 11, and 8 – 13. For the second community cluster, only the 1 – 7 community pair demonstrated a significant simple interaction at Session 2. **(d)** There were no community pairs that demonstrated a significant simple interaction between MOTOR and VISUAL factors after a one-week no-training delay at Session 3.

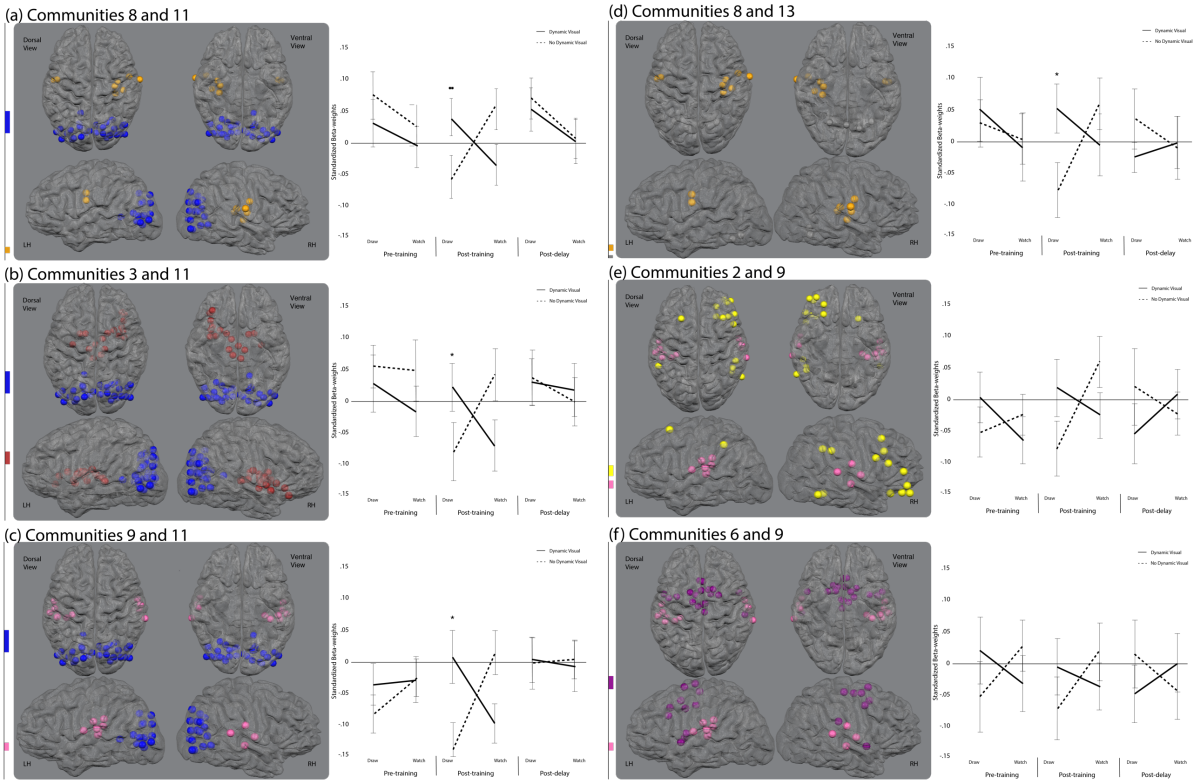

Figure 27. Training-related Changes in Functional Connectivity for Cluster 1. Six community pairs in cluster 1 demonstrated a significant interaction between MOTOR (draw, watch) and VISUAL (dynamic visual, no dynamic visual) at Session 2 that was found at neither Session 1 nor Session 3. Significant interactions were followed with planned paired t-tests. **(a, b, c)** Three communities demonstrated significant differences in their functional relationship with community 11, a community comprised of nearly entirely visual ROIs. Communities 8, 3, and 9 are made of bilateral ventral somatomotor ROIs, subcortical ROIs, and bilateral auditory cortex. **(c, e, f)** Three communities demonstrated significant differences in their functional relationship with community 9, a community comprised of auditory ROIs. These include communities, 11, 2, and 9. Community 2 is comprised of frontal and parietal ROIs and is largely right-lateralized. Community 6 is comprised of primarily of bilateral frontal motor regions. **(a, d)** Two communities demonstrated differences in their functional relationship with community 8. These include communities 11 and 13. Community 13 is comprised of 4 cerebellar regions. ** $p < .01$, * $p < .05$.

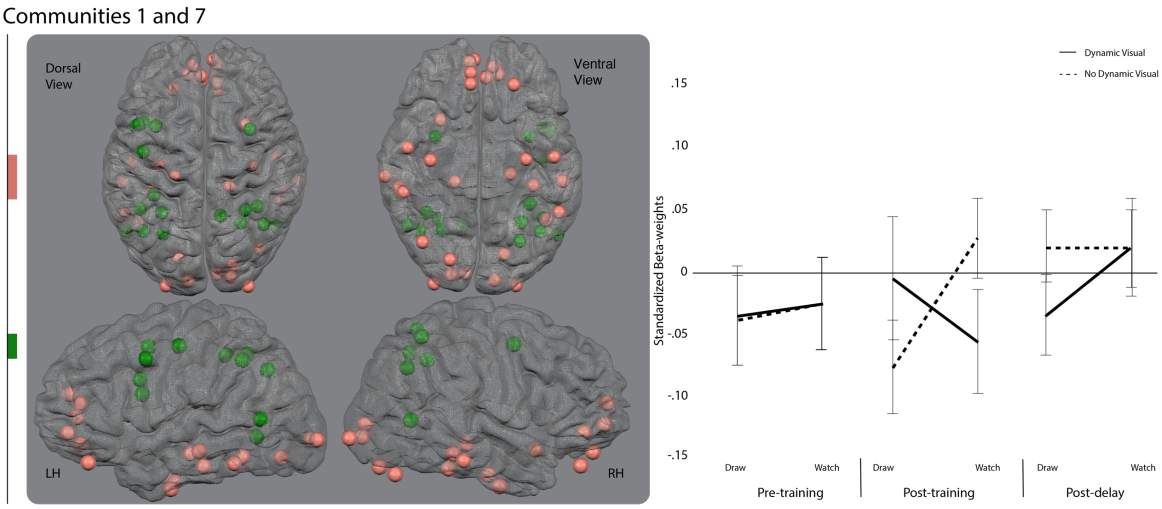

Figure 28. Training-related Changes in Functional Connectivity for Cluster 2. Only one community pair in cluster 1 demonstrated a significant interaction between MOTOR (draw, watch) and VISUAL (dynamic visual, no dynamic visual) at any session. The interaction was significant at Session 2 but not at Sessions 1 or 3. None of the planned paired t-tests were significant. Community 1 was comprised of ventral-temporal and prefrontal ROIs and was largely similar to Unknown community in the original Power et al. (2011) partition. Community 7 was comprised of frontal and parietal ROIs.

Discussion

Letter production is a sensorimotor activity that relies upon a tight coupling between motor movements and visual feedback in the early stages of letter learning. This chapter explored the importance of this visual-motor coupling to (1) gains in letter recognition and (2) the emergence of visual-motor functional connectivity during letter perception. I hypothesized that the spatiotemporal contingency among the motor and visual experiences of the letter during letter production would lead to gains in recognition and the emergence of visual-motor functional connectivity during visual perception. The results support these hypotheses. Participants recognized symbols learned by drawing them with ink faster than symbols learned in other conditions where motor and visual experiences were not coupled, such as drawing symbols without ink or simply watching them unfold as if they were being written. Participants also demonstrated changes in functional connectivity among visual, motor, and (surprisingly) auditory neural communities that were associated with the contingency between the visual and motor experiences during letter production. After a week-long no-training delay, participants were still better at recognizing symbols learned by drawing them with ink but the functional connections observed immediately after training had returned to their pre-training baseline. Taken together, these results suggest that the visual-motor functional connectivity observed during perception after symbol production training was not directly related to the concurrent gains in recognition.

Recognition

My hypothesis was that the contingency between the visual and motor experiences of a letter that occur during letter production is important for the gains in letter recognition that often follow letter production training (Longcamp et al., 2005; Zemlock et al., 2018). I predicted that symbols learned through draw with ink training would be recognized better than symbols learned in draw no ink, watch dynamic, and watch static training because draw with ink training was the only condition that explicitly coupled the visual and motor experiences of the symbol. I found that participants did, indeed, recognize symbols better when they had been learned through draw ink training than any of the other training conditions. I interpret these results to indicate that the contingency between the visual and motor

experiences of a letter that occur during letter production is an important part of why letter production results in gains in letter recognition.

Several other works have demonstrated similar recognition gains after production practice for letters in preschool-aged children (Longcamp et la., 2005; Zemlock et al., 2018) and for novel symbols in adults (Longcamp et al., 2006, 2008). These studies have collectively demonstrated that production practice increases recognition for the practiced forms relative to typing and visual-only training, suggesting that the benefits of production on recognition were not simply due to the positive effects of motor actions (i.e., typing) on the orienting of attention or to visual exposure alone. The results of the current study extend these findings by demonstrating that one reason that production practice facilitates learning more than typing or visual-only training is because production requires a spatiotemporal coupling between the visual and motor experiences of the form produced.

The current study also demonstrated that recognition gains were present immediately after training and were maintained to a certain degree after a one-week no-training delay. This result is in line with prior work demonstrating that recognition gains for production over typing experience were evident immediately after training ended and after a one-week no-training delay in preschool-aged children (Longcamp et al., 2005) and in literate adults (Longcamp et al., 2008). These results are also in line with prior work demonstrating that training-induced changes in recognition decrease monotonically after training ceases (Longcamp et al., 2006).

Functional Connectivity

My hypothesis for functional connectivity was similar to my hypothesis for recognition: the contingency between the visual and motor experiences of a letter that occur during letter production is important for increases in functional connectivity between visual and motor brain system during letter perception (Chapter 2). This hypothesis was addressed with two primary predictions: (1) training will affect connectivity among visual and motor brain regions, specifically, and (2) functional connectivity will be more positive for draw ink training than all other training conditions. Each be addressed in turn.

First, I predicted that draw with ink training would change functional connectivity among visual and motor brain systems during symbol perception more than draw no ink, watch dynamic, or watch static training. I, therefore, looked for functional connections among neural communities that demonstrated an interaction at the post-training scan that was not present at the pre-training scan. I found that two clusters of community pairs demonstrated an interaction at post-training that was not present at the pre-training scan. The first cluster was largely comprised of primary sensory regions (visual, auditory) as well as frontal motor regions, cerebellar, and subcortical regions (Figure 27). The visual and auditory communities were both central to this cluster, both being associated with at least three other communities in the cluster. This cluster can therefore be summarized as a functional network comprised of primary sensory and motor-related regions. The second cluster was comprised of ventral-temporal regions as well as parietal and frontal motor regions and can be summarized as a functional network comprised of ventral-temporal, parietal, and frontal motor regions (Figure 28). These results, therefore, were generally in line with the prediction that the functional networks affected would be related to visual and motor brain regions, though other functional connections were also affected.

Second, I predicted that functional connectivity would be more positive for symbols trained through draw with ink training than symbols trained through draw no ink, watch dynamic, and watch static training. The results were not in line with this prediction, however. Functional connectivity was *not* more positive for symbols trained through draw with ink training than symbols trained through draw no ink, watch dynamic, and watch static training. Symbols trained through draw with ink and watch static training both resulted in similarly positive levels of functional connectivity in both clusters and were often no different than zero (Figures 27 and 28). The interactions were generally due to negative functional connectivity for symbols learned through draw no ink and watch dynamic training. This suggests that the interaction between visual and motor factors after training was due to a decoupling of neural systems during the perception of symbols learned through draw no ink and watch dynamic training. The results, therefore, are not in line with the prediction that draw ink training would *increase* functional connectivity during perception but do not necessarily invalidate the hypothesis that the visual-motor coordination

inherent to letter production leads to the emergence of visual-motor functional connectivity during letter perception.

It is important to remember that this study was conducted with literate adults who have likely already established functional networks for learning through visual-motor activities. Both Clusters 1 and 2 are likely established functional networks that routinely support visual-motor activities and expect certain spatiotemporal contingencies. Interpreting the results with this in mind, the findings that draw no ink and watch dynamic training led to a negative relationship among motor and primary sensory systems (cluster 1) suggests that training with de-coupled visual and motor experiences facilitated a de-coupling among sensory and motor systems that would, otherwise, have continued their general function. This would explain why we found no difference in functional connectivity between draw ink and watch static at the post-training scan and why the pre- to post-training changes from draw ink and watch static generally appeared small relative to the changes from draw no ink and watch dynamic (although this was not directly tested). This interpretation receives some support from studies demonstrating that learning a new task utilizes pre-existing neural patterns, at least in cases where the new task is similar to a learned task (e.g., finger sequencing) (Sale, Reid, Cocchi, Pagnozzi, Rose, & Mattingley, 2017). In this case, the draw with ink and watch static training are both tasks that participants had likely experienced often and resulted in the 'normal' patterns of functional connectivity that would accompany symbol learning in adults through these tasks. Draw no ink and watch dynamic, however, were likely more novel tasks for adults and resulted in a disruption of the 'normal' patterns of connectivity. Future work should investigate changes in functional connectivity in young children to determine if these training conditions have different effects in young children who may still be learning about the expected spatiotemporal contingencies and, perhaps, learning how to learn from them.

Relationship Between Functional Connectivity and Recognition

My hypothesis was that functional connectivity does not directly support gains in recognition but that it might translate to gains in recognition by facilitating the development of some other neural mechanism. Although this study could not address this hypothesis fully, it was able to characterize the

time scale of training-induced changes in functional connectivity and recognition to provide evidence in support of the notion that training-induced changes in functional connectivity are not, in and of themselves, supporting training-induced changes in recognition. I predicted that any training-induced functional connections found at the post-training scan would not be present after the one-week no-training delay but that the recognition gains would be maintained. I found, as predicted, that the patterns of functional connections found at post-training were no longer present at post-delay and that changes in recognition were maintained to a certain degree over the no-training delay. The results, therefore, were in line with my predictions and provide support for the notion that training-induced changes in functional connectivity do not *directly* support changes in recognition.

An additional finding supports the notion that the emergence of visual-motor functional connectivity at post-training did not directly support the gains in recognition that were observed at post-training. Training produced an ordinal interaction between the visual and motor factors for recognition while training produced a cross over interaction for functional connectivity. Recognition for symbols learned through draw with ink training was better than recognition for symbols learned in any of the other three training conditions. Functional connectivity, however, was greater for draw with ink training when compared to training with only the motor component (i.e., draw no ink) or with only the visual component (i.e., watch dynamic) but was no different than training with neither (i.e., watch static). This suggests that at least two mechanisms were at work and, in fact, provides further support for the hypothesis that training-induced patterns of functional connectivity during perception affect the development of some other neural mechanism that supports recognition because training conditions had different effects on functional connectivity than they did on recognition.

The Potential Role of the Two Clusters in Perceptual Learning from Sensorimotor Experiences

Spatiotemporal contingencies among sensory and motor experiences define all of our interactions with the world. There is hardly an action that does not elicit a sensory consequence—hardly a sensation that does not elicit an action. All of these sensorimotor pairings had to be learned—we did not always know that the somatosensory and visual sensations that accompany drawing the letter “A” with a pen.

After a history with these sensorimotor contingencies, sensorimotor cycles are built and within these cycles is an expectation that certain actions correspond to certain sensations and certain sensations correspond to certain actions. This study demonstrates that two functional networks were affected by experiences that violate what would be an expected contingency between visual and motor experiences during letter production. Neither draw ink nor watch static training would violate an expected contingency and neither condition appeared to affect the functional connectivity in these functional networks. I suggest that the state of these sensorimotor networks during the perception of symbols that had been learned through draw ink and watch static training was simply the continual functioning of a sensorimotor learning network that has two relatively independent learning mechanisms. In what follows, I speculate on the potential contribution of these two functional networks to symbol learning.

The results of Chapter 5 suggested that ventral-temporal cortex may be affected by letter production differently than the dorsal motor system. I speculated that early letter production may not be under perceptual guidance, yet, but may be sufficiently guided by vision and visual-motor processes because letter production is, essentially, a copying task in the early stages of learning—it does not require the participant to 'know' the form. I suggested that, perhaps, two sensorimotor networks were affected by letter production, one being directly affected by the actual motor movements and another being indirectly affected through the visual percepts created during letter production. It is interesting to note that the major difference between the two clusters that were affected by training is that one cluster contained primary visual cortex (cluster 1) and the other contained ventral-temporal cortex (cluster 2).

Although, I reiterate, speculative, cluster 1 may be related to changes in functional connectivity that occurred early in the training to support the early stages of symbol training that were closer to a symbol copying task. Cluster 1 would, then, be a sensorimotor network that supports visual-motor and motor processes when perceptual guidance is not necessary or not yet available. Cluster 2, on the other hand, may be related to changes in functional connectivity that occurred later on in training to support the later stages of symbol training that were closer to symbol production. Cluster 2 would, then, be more of a

visual-perceptual-motor network that, first, learns from the outputs of cluster 1 and, then, provides perceptual guidance during production.

Cluster 2 was, furthermore, the only community pair to demonstrate a trend towards a unique effect on functional connectivity for the draw ink condition at either post-training or post-delay sessions. This cluster is, therefore, the only community to demonstrate anything close to the same training effects for functional connectivity as for recognition. Cluster 2 demonstrated a trend toward an ordinal interaction for functional connectivity at the post-delay session, with similar, positive functional connectivity values for all conditions besides draw with ink. Consider that no communities in cluster 1 resulted in anything trending towards an effect for draw ink compared to the other three conditions at either post-training or post-delay. Cluster 2, however, demonstrated a trend towards this pattern at the post-delay scan. Given the abundance of research suggesting a role for ventral-temporal cortex on object perceptual processes and the possibility that it may function relatively autonomously during perception in later stages of learning (Gauthier, 2000; Gauthier, Tarr, Andersen, Skudlarski, & Gore, 1999; Grill-Specter & Weiner, 2014; Haxby et al., 2001; Malach, Levy, & Hasson, 2002; Milner & Goodale, 2006; Ungerleider & Mishkin, 1982), cluster 2 may be related to perceptual processes—it may be best at perceptual processes when it *isn't* coupled with the fronto-parietal system. This suggests that functional connectivity with ventral-temporal cortex is actually associated with lower recognition performance. Although speculative at best, this interpretation would be in line with several studies that have demonstrated that functional connections decrease as performance increases (Andres et al., 1999; Bassett et al., 2015). It is also in line with the proposition that ventral-temporal cortex 'learns' faster than the dorsal motor system (Chapter 5)—cluster 2 demonstrated potential for a learning effect at the post-delay scan whereas cluster 1 demonstrated no potential for a learning effect at either post-training or post-delay.

Conclusion

This dissertation has been concerned with understanding the neural mechanisms that support changes in letter perception that occur as a consequence of experience with letter production and what it is about letter production that might cause these changes. We have demonstrated that (1) visual-motor

functional connectivity supports letter production (Chapters 3 and 4) and that (2) experience with letter production leads to visual-motor functional connectivity during letter perception in preliterate children (Chapter 2). The experiment described in this chapter demonstrates that the precision of the match between sensory and motor experiences contributes to the state of sensorimotor functional networks in the brain during letter perception and also contributes to gains in visual letter recognition. The results of the current study suggest, however, that the emergence of visual-motor functional connectivity during letter perception may not directly support gains in recognition.

It is possible that the emergence of visual-motor functional connectivity during letter perception is related to changes in perceptual processing other than recognition, such as categorization or other more implicit perceptual processes. This is unlikely, however, given the results reported in Chapters 4 and 5. Chapter 4 reported null effects for several direct tests of functional connectivity during letter perception in literate adults. Literate letter perception is characterized by automatic letter recognition and finding no evidence of functional connectivity during letter perception in literate adults suggests that functional connectivity is not necessary for visual recognition—and further indicates that it is not necessary for visual letter perception because we did not isolate letter *recognition*, we only isolated letter perception. Because the in-scanner task in Chapter 4 was simply passive visual perception, finding no evidence of functional connectivity during letter perception suggests that functional connectivity is not necessary for perception, broadly, and not just that it's not necessary for recognition. Chapter 5, on the other hand, reported that a distributed set of brain regions, including ventral-temporal, parietal, and frontal motor regions, was active during letter perception in literate adults and, therefore, during letter perception. Chapters 4 and 5, together, suggest that activation in these regions may support letter perception but that functional connectivity among them is not strictly necessary for perceptual processes.

The findings of the experiment in this chapter support the notion that a visual-motor functional network is only present during object perception shortly after sensorimotor experiences with that object and would be in line with theories that suggest that functional networks that support certain experiences continue to reverberate after the experience ends but gradually decrease as time passes (Alvarez & Squire,

1994; Hebb, 1949). They would be at odds with theories that suggest that these reverberations are the neural representations supporting perceptual processes (McClelland et al., 1995; Versace et al., 2009), at least recognition processes, because recognition gains persisted even as functional connectivity changes faded. These findings would be more in line with theories that suggest that these reverberations merely contribute to the development of other neural processes that underlie perceptual processes (Aizawa et al., 1991; Freeman, 1995). And, considering the results of Chapter 3, 4, and 5, suggest that these reverberations are contributing to the development of more localized processes that support perception.

CHAPTER 7:

GENERAL DISCUSSION

Summary of Main Findings

The work described in this dissertation focused on understanding the neural mechanisms that underlie changes in letter perception after letter production practice. It explored the relationship between letter production and communication among sensory and motor brain regions during letter production and during subsequent letter perception with an emphasis on the perceptual process of recognition in the sensory modality of vision. The hypotheses of this dissertation have been that (1) the visual-motor coordination inherent to letter production coordinates neural activity among visual and motor brain regions during letter production, that (2) this visual-motor coordination during letter production contributes to the emergence of visual-motor functional connectivity during letter perception, and that (3) the emergence of this visual-motor functional connectivity during perception supports gains in visual letter recognition. These three hypotheses were formulated based on the proposal that the manipulation of a specific object coordinates visual-perceptual, visual-motor, and motor activity in the brain and that this neural linking is supportive of developmental changes in object perception.

Chapters 3 and 4 provided support for the first hypotheses—that the visual-motor coordination inherent to letter production coordinates neural activity among visual and motor brain regions *during letter production*. We predicted that a ventral-temporal, parietal, and frontal motor functional network would support letter production in literate adults. We, first, demonstrated that neural activity in ventral-temporal, parietal, and frontal motor brain regions could be coarsely related to the visual-perceptual, visual-motor, and motor components of letter production, respectively (Chapter 3). Neural activity in ventral-temporal cortex was associated with the visual-perceptual component of letter production, the visual experience of the letter unfolding as it is being produced. Activity in posterior parietal cortex was associated with the visual-motor component of letter production, the online use of vision to guide movement. Activity in frontal motor regions was associated with the motor component of letter production, the motor experience of movements performed to produce the form. We, then, investigated

functional connectivity among the visual and motor brain regions that supported letter production in literate adults (Chapter 4). We found that motor component of letter production was associated with fronto-parietal connections while the visual component was associated with ventral-temporal-parietal connections as well as ventral-temporal-frontal connections and a fronto-parietal connection. These results demonstrated that visual and motor systems coordinate their activity during letter production and that the contingency between the visual and motor experiences during production affects this visual-motor functional network during production.

Chapters 2 and 6 provided support for the second hypothesis—that visual-motor coordination during letter production contributes to the emergence of functional connectivity among visual and motor brain regions *during letter perception*. In Chapter 2, we predicted that experience with letter production would result in the onset of functional connectivity among ventral-temporal, parietal, and frontal motor brain regions during subsequent letter perception in preliterate children. We found that, relative to typing practice, letter production and tracing practice increased functional connectivity among ventral-temporal and primary motor cortices during subsequent letter perception. We found that any training led to functional connectivity among ventral-temporal and parietal cortices and suggested that, because all training conditions were visual-motor in nature (i.e., production, tracing, typing) that all training conditions led to changes in functional connectivity with parietal cortex. In Chapter 6, we directly manipulated the coordination between visual and motor experiences during production in adults learning novel symbols. We predicted an increase in functional connectivity among visual and motor brain regions during the perception of symbols learned in training conditions that maintained the coordination between visual and motor experiences during production. Results were slightly different than predicted—symbols learned in training conditions that disturbed the coordination between visual and motor experiences led to a decoupling among sensory and motor neural systems—but would be in line with the hypothesis that visual-motor coordination during letter production changes functional connectivity among visual and motor brain regions during subsequent perception.

The results of the experiments reported in Chapters 4 and 5 provided unexpected information concerning the role of visual-motor functional connectivity in letter perception. Chapter 4 found no evidence for functional connectivity during letter perception in literate adults, suggesting that functional connectivity does not directly support letter perception. Chapter 5 suggested that perceptual processes in ventral-temporal cortex may develop somewhat independently of more motor-oriented processes in parietal and frontal motor cortices, suggesting, in the least, that the participation of visual and motor brain regions in visual letter perception may develop on different time scales. If functional connectivity during perception supported recognition in and of itself, as originally hypothesized, then we should have found evidence for functional connectivity during perception in literate adults and a similar developmental trajectory for visual and motor brain regions during perception.

Chapter 6 provided support for a modified version of the third hypothesis—that the emergence of this visual-motor functional connectivity during perception translates to gains in visual letter recognition by contributing to the development of some other neural mechanism. The experiment reported in Chapter 6 was not able to directly assess a causal relationship between visual-motor functional connectivity during perception and gains in visual letter recognition but, rather, provided evidence for the supporting claim that training-induced changes in functional connectivity do not directly support changes in recognition. Chapter 6 demonstrated that training-induced changes in functional connectivity were qualitatively different than training-induced changes in recognition. Functional connectivity was no different between symbols learned through production and symbols learned by passively perceiving handwritten symbols. Recognition, however, was greater for symbols learned through production than symbols learned by passively perceiving handwritten symbols. Changes in functional connectivity, furthermore, were not maintained over a one-week no-training delay while changes in recognition were maintained. Chapter 6, therefore, demonstrated that visual-motor functional connectivity does not, in and of itself, support recognition, but leaves open the possibilities that visual-motor functional connectivity supports some other perceptual process than recognition specifically and that visual-motor functional connectivity might contribute to the development of other neural mechanisms that support perceptual processes.

There were two additional hypotheses that were addressed by this dissertation. These hypotheses were corollaries of the original three hypotheses: (4) letter production and letter perception are supported by a similar visual-motor functional network and (5) visual-motor coordination during letter production supports gains in visual letter recognition.

Chapter 4 directly tested (4) by measuring visual-motor functional connectivity during letter production and letter perception in the same participants. We found that a functional network comprised of ventral-temporal, parietal, and frontal motor regions supported letter production, but we found no evidence of functional connectivity during letter perception. We were, therefore, unable to compare functional connectivity during letter production to functional connectivity during letter perception. The results were clear, however: letter production and letter perception are *not* supported by a similar visual-motor functional network. Finding no functional connectivity during letter perception was unexpected, given that Chapter 2 reported visual-motor functional connectivity during letter perception after letter production in preschool children, but indicates that the emergence of visual-motor functional connectivity may be characteristic of the early stages of letter learning and not later stages or, perhaps, is reliant on a within-experiment training manipulation.

Chapter 6 directly tested (5) by training adults on novel symbols through different manipulations of the visual and motor experiences of these forms that would occur during production. Participants were better at recognizing symbols learned when the visual and motor experiences were coordinated than in any of the control conditions after only one day of training. The additional three days of training did not change the difference between recognition for these symbols relative to control symbols and, further, recognition gains were maintained over a one-week no-training delay. The results, therefore, supported the hypothesis that visual-motor coordination during letter production supports gains in visual letter recognition and add that these recognition gains occur relatively quickly and are maintained for at least one week.

The body of work described in this dissertation, therefore, supports the proposal that the manipulation of a specific object coordinates visual-perceptual, visual-motor, and motor activity in the

brain and that this neural linking is supportive of developmental changes in object perception. Although we were unable to find direct evidence for the role of neural linking among visual-perceptual, visual-motor, and motor brain systems in visual perception, we were able to demonstrate that one action that explicitly couples visual and motor experiences (i.e., letter production) of an object (i.e., letters) changes the communication patterns among brain regions that are associated with the visual-perceptual, visual-motor, and motor components of that action during subsequent visual perception of that object. We also demonstrated that the coupling between visual and motor experiences is the property of that action that leads to gains in subsequent visual recognition of that object. Actions that explicitly couple visual and motor systems, therefore, coordinate neural activity among these systems during the action and contribute to the onset of a visual-motor functional network that may not directly support object perception but that may, nonetheless, contribute to the development of object perception.

In what follows, I address some of the unexpected results and their implications for the three original hypotheses of this dissertation. The first of these unexpected results is an apparent absence of functional connectivity during adult letter perception. This particular unexpected result is the most problematic for the original hypotheses and, in fact, led to a mid-dissertation change in the third original hypothesis. The second of these unexpected results is the finding that ventral-temporal cortex responds at an earlier age than parietal and motor regions during letter perception. The particulars of this result suggested, further, that ventral-temporal development may be under different influences than fronto-parietal development. I will end by focusing on the broader implications of the work described in this dissertation for our understanding of brain development from sensorimotor experiences. I, in particular, propose that the ongoing functional dynamics of well-documented brain networks may only appear established because they are responding to consistent environmental influences and that objects may play a central role in their maintenance.

Absence of Functional Connectivity During Adult Letter Perception

Prior work demonstrated that letter production increases letter recognition ability (Longcamp et al., 2005, 2006, 2008; Zemlock et al., 2018) and leads to an increase in activation in visual and motor

brain regions during letter perception in preliterate children (James & Engelhardt, 2012; Kersey & James, 2013) and in literate adults learning novel symbols (James & Atwood, 2009). These authors have interpreted these findings to suggest that a sensorimotor network supports the gains in letter recognition that follow letter production training. In line with these authors, we originally hypothesized that letter production would lead to functional connectivity among visual and motor brain regions and that this would support gains in letter recognition. Chapter 2 demonstrated that a sensorimotor network does indeed support letter perception in preliterate children after production training but did not provide information concerning the role that this sensorimotor network might play in letter recognition. Chapter 4 reported null effects for several directs tests for a sensorimotor network during letter perception in literate adults. The results of the experiment in Chapter 4 were, therefore, unexpected because they suggested that a sensorimotor network is not necessary for letter perception in literate adults.

Although unexpected, an apparent absence of functional connectivity during literate letter perception is not necessarily inconsistent with the prior literature on letter perception and, more broadly, on object perception. Visual object perception has been a highly researched topic for several decades, often focusing on perceptual processes in ventral-temporal cortex (Gauthier, 2000; Gauthier et al., 1999; Grill-Specter & Weiner, 2014; Haxby et al., 2001; Malach, Levy, & Hasson, 2002; Milner & Goodale, 2006; Ungerleider & Mishkin, 1982). Early work in this field was strongly suggestive of localized processing for visual object perception (e.g., Gauthier et al., 1999, Kanwisher et al., 1997; Malach et al., 1995; Puce et al., 1996) and has, more recently, demonstrated that visual object perception activates several brain regions (e.g., Culham & Kanwisher, 2001; Gauthier et al., 2000; Grill-Spector, Kourtzi, & Kanwisher, 2001) that are, perhaps, connected by underlying white matter structure (Saygin et al., 2012; Osher et al., 2016). Brain regions that respond during passive object perception often include areas in ventral and dorsal visual streams as well as frontal motor cortex (Grèzes & Decety, 2002; James & Gauthier, 2006; Sim, Helbig, Graf, & Kiefer, 2015). Most authors have interpreted this as evidence that a distributed neural system supports object perception with different areas performing different processes (e.g., Culham & Kanwisher, 2001; Grèzes & Decety, 2002; James & Gauthier, 2006; Saygin et al., 2012;

Sim et al., 2015; Osher et al., 2016) as opposed to a distributed neural system that are, collectively, performing one processes. Some of these authors suggest that the different processes are carried out relatively independently from one another (e.g., Culham & Kanwisher, 2001) and others suggest that the different processes must be coordinated for adaptive behavior and, therefore, these brain regions must be communicating with one another (e.g., Grèzes & Decety, 2002; James & Gauthier, 2006; Sim et al., 2015). Although theories such as these have been around for quite some time and work in this field continues to have momentum, I am not aware of any body of work that is investigating the functional networks supporting visual object processing using measures of task-based functional connectivity.

In any case, finding no evidence of functional connectivity during letter perception in literate adults suggested that functional connectivity among visual and motor regions is not necessary for letter recognition. I, therefore, abandoned my original hypothesis, and in Chapter 4, I hypothesized that functional connectivity may, instead, support the development of other neural mechanisms that support changes in letter perception. The experiments reported in this dissertation do not directly address this new hypothesis, but they provide some loose support for what other neural mechanisms might be affected by functional connectivity during learning. There is some support from the studies in this dissertation for the mechanisms being relatively localized processes and some support for the mechanism being another functional network or other functional networks, plural. I will discuss the support for both of these possibilities below.

Support for the mechanisms being relatively localized processes comes from comparing the studies that used activation as a dependent measure (Chapters 3 and 5) to studies that used functional connectivity (Chapters 2 and 4) during letter perception. Activation in a distributed set of brain regions, including ventral-temporal, parietal, and frontal motor regions, supported letter perception in literate adults (Chapter 5), consistent with prior work (James & Gauthier, 2006; Longcamp et al., 2003, 2008). Activation in only ventral-temporal cortex supported letter perception in children and there was no evidence of activation in younger children who had, at their young age, very little experience with letters (Chapter 5). Chapter 5, therefore, demonstrated that more brain regions demonstrate activation during

letter perception as age increases (Chapter 5). James and Engelhardt (2012) demonstrated that giving children experience with letter production results in more brain regions demonstrating activation during letter perception. Activation in ventral-temporal, parietal, and frontal motor brain regions, therefore, increases with age, likely due to experience with letter production, and is not observable before production experience.

Functional connectivity during letter perception appears to be more similar to activation in the early stages of learning than in later stages. Functional connectivity among ventral-temporal, parietal, and frontal-motor regions was present after production practice in preliterate children (Chapter 2)—it emerged at the same time that activation in these regions emerged. Note that activation during letter perception did not occur in young children before training (Chapter 5). Functional connectivity and activation, therefore, come online together during early learning. They do not appear to stay together throughout development, however. Functional connectivity among these regions was not present during letter perception in literate adults (Chapter 4) but activation was (Chapter 5). It is particularly telling, then, that we found that activation in this distributed set of regions did not all emerge at once. We found that literate children responded to letters in ventral-temporal cortex while literate adults demonstrated the distributed ventral-temporal-front-parietal response (Chapter 5). Taken together, this suggests that functional connectivity may contribute to the development of more localized processes that, at a certain point in development, no longer need to communicate with one another to support perception.

Functional connectivity during learning may, on the other hand, be contributing to developmental changes in the functioning of other functional networks that support perceptual processes. Support for this possibility comes from the results of the experiment reported in Chapter 6. Chapter 6 reported two functional networks that were affected by letter production training. Neither of these functional networks demonstrated change in functional connectivity that mirrored the changes in recognition, but one of the functional networks came close. It is possible that, with more participants or with a shorter/longer delay, functional connectivity with ventral-temporal cortex may have mirrored changes in recognition. The finding would be that recognition is better when ventral-temporal cortex is less connected with parietal

and frontal motor systems and would suggest that the developmental effect is one of segregation and leads towards the development of more localized processing. The 'localized' process here, however, would include a functional network that encompasses nearly all of ventral-temporal cortex, suggesting that ventral-temporal cortex may contain within itself functional networks that support object perception. This would be consistent with theories of ventral-temporal function and object perception, such as object form topography (Haxby, Ishai, Chao, Ungerleider, & Martin, 2000), and would suggest that functional networks that are widespread through cortex contribute to the development of functional networks within ventral-temporal cortex that support object perception.

Whether or not functional connectivity contributes to localized processes or more distributed network processes, it is clear that the onset of a sensorimotor network after production training has a more complex relationship with gains in perception than I had originally hypothesized. More work will be necessary to better understand the relationship between training-induced changes in functional connectivity and recognition that both occur after production. It appears most likely, from the collective results of this dissertation, that functional connectivity may contribute to the development of more localized processes that support perception, perhaps functional networks contained within ventral-temporal cortex.

Different Developmental Timescales for Dorsal and Ventral Involvement in Perception

One of my original hypotheses was that visual-motor experiences with letters would lead to visual-motor functional connectivity during subsequent letter perception. I had no original hypotheses concerning how this visual-motor functional connectivity might affect local activity in the brain regions that it 'connects'. Latent in my original hypothesis was the expectation that the coordination between these dorsal and ventral visual streams with motor cortex would contribute to a co-development of visual and motor brain regions—that local activation in these regions would have similar developmental trajectories because of their coordination. Several activation studies have demonstrated that activation in the entire sensorimotor system emerges together after within-experiment manipulations (James & Engelhardt, 2012; James & Atwood, 2009; Kersey & James, 2013). Finding that training-induced changes

in activation during letter perception were, indeed, due to an underlying sensorimotor network appeared to suggest that these regions may co-develop through the coordination of their activity with one another (Chapter 2). The findings in Chapter 5 demonstrate, on the contrary, that activations in dorsal and ventral visual streams and motor cortex during letter perception do not all emerge at the same age.

There are, at least, two non-mutually exclusive avenues through which changes in dorsal and ventral visual streams might occur from letter production experience. The first of these related to the motor component of letter production. Motor movements generate a great deal of efferent neural activity, sending neural output from primary motor cortex to several other brain regions, most notably frontal premotor regions and parietal cortex (for review see Ostry & Gribble, 2015). In auditory-speech learning, for instance, long-term changes in auditory perceptual judgements were related to the sounds participants actually produced during training and not the manipulated auditory feedback provided to them (Lametti, Rochet-Capellan, Neufeld, Shiller, & Ostry, 2014), suggesting that changes in motor and somatosensory activity that coordinate sound production and throat sensations supported the learning. The second is related to the visual-perceptual component. Motor learning activities create environmental realities that are, in turn, processed by sensory systems and, therefore, lead to perceptual changes. Letter production is one such case. Perceptual gains from visual-only learning in young children were just as large as the gains from letter production learning if variability was introduced into the visual exemplars (Li & James, 2016), suggesting that changes in visual perceptual activity supported the learning. Changes in visual perception can, then, occur through efferent neural communication from motor cortex that occurs due to the movement or through the visual percepts created during production.

Differences in the development of ventral and dorsal stream functioning could be due to differences in the effects of functional connectivity or to differences in the effects of visual-perceptual input. Differences in the development of these two streams could, of course, be due to any pairing of functional connectivity and visual input effects. Functional connectivity could, for instance, have negligible effects on ventral-temporal cortex but larger effects on parietal functioning. Changes in ventral-temporal cortex would, in this scenario, be driven by the visual-perceptual inputs. It could also be that

functional connectivity has similar effects on both streams, but that visual inputs affect only ventral-temporal cortex. Or, functional connectivity may contribute to ventral stream processes before it begins to contribute to dorsal stream processes. There are many pairings of these two developmental influences that might lead to differences in the developmental trajectories of ventral and dorsal visual streams during perception and these pairings could have different effects at different developmental time points. I will, however, focus on early learning and on one pairing that I find most plausible.

Visual-perceptual processes in the ventral visual stream may develop somewhat independently of more motor-oriented processes in the dorsal visual stream and frontal motor cortices. While more motor-oriented processes the dorsal stream may be more reliant upon functional connectivity among parietal and frontal motor cortex, visual-perceptual processes in the ventral visual stream may be more affected by the visual perceptual outputs created by motor actions. Such an explanation would be at odds with the expectation latent in the original hypothesis that visual and motor brain regions would co-develop as they coordinated their activity with one another during sensorimotor experiences but more consistent with the collective results of the experiments reported in this dissertation. This explanation would suggest that, instead of co-developing through coordinated neural activity, they would co-develop as complementary systems. The dorsal visual stream and motor system interact with objects in ways that are conducive to the ventral visual stream learning them.

The major environmental change effected by letter production is the creation of a handwritten version of the letter that persists after the letter production episode has finished. This visual input may be responsible for the changes in ventral-temporal function after letter production. Ventral-temporal cortex is broadly associated with object categorization processes (for review see Grill-Spector & Weiner, 2014), and the development of object categorization processes is largely driven by the perceptual differentiation that follows exposure to category variability (Li & James, 2016; Perry et al., 2010; Twomey et al., 2014a, 2014b). The particulars of the results reported in Chapter 5 suggest that ventral-temporal cortex may be most sensitive to the variability present in handwritten forms when children are first learning about letters

and that this sensitivity to variability may be a part of how ventral-temporal cortex undergoes developmental changes that contribute to the formation of category-selective responses.

The response in frontal motor and parietal cortices during letter perception, on the other hand, may be most associated with the strong interconnectivity between these regions during the motor action itself (for review Nakamura & Koudier, 2003; Katanoda et al., 2001; Rizzolatti et al., 1998; Yuan & Brown, 2015). In younger children, who may not have developed motor plans or programs for motor production, actions themselves may require efficient use of visual and somatosensory feedback throughout the letter production episode (Palmis, Danna, Velay, & Longcamp, 2017). With each letter produced this visual-somatomotor connectivity is strengthened and refined, resulting in a somatomotor representation (motor plans/programs) tied to the dorsal visual system, not the ventral visual system, that can be called upon when simply presented with the visual cues for motion that are typically experienced during the visual-motor activity.

The response in frontal motor and parietal cortices during letter perception in literate adults might, therefore, develop through the experience of the motor movement itself whereas the response in the ventral temporal cortices might develop through the visual perceptual experiences created by letter production. This suggestion is supported by the two visual steams hypothesis that proposes differing developmental time courses for ventral and dorsal stream processes (Goodale & Milner, 2005; Milner & Goodale, 2006; Stiles et al., 2013) and connectivity between these systems (Fair et al., 2008; Lebel et al., 2008) in the context of a breadth of literature documenting strong somatomotor interconnectivity between motor and parietal cortices (Andersen, Asanuma, Essick, & Siegel, 1990; for review on written production Nakamura & Koudier, 2003; Ostry & Gribble, 2015; Petrides & Pandya, 1984; Guye et al., 2003).

Chapter 6 also provides some preliminary evidence for two complementary learning systems during letter production. Two relatively independent functional networks were affected by training with unexpected sensorimotor contingencies. The first of these was a large fronto-parietal system that also included primary visual and auditory cortices. This functional network may be related to a more motor-

oriented learning system that learns to efficiently integrate somatosensory and visual information to control motor movements. The second of these was a smaller network comprised of a few fronto-parietal regions as well as ventral-temporal cortex. This functional network may be related to a more perceptual-oriented learning system that is more focused on learning to differentiate among objects. Sensorimotor learning activities are often found to be better at inducing learning effects than other unimodal activities (see Shams & Seitz, 2008 for review), perhaps because of their ability to effect local neural activity in both of these systems, resulting in developmental changes in more motor-oriented dorsal stream and frontal regions and, also, in more perceptual-oriented ventral visual stream regions.

That sensitivity to letter category in parietal and motor cortices was only present in the literate adults suggests that the parietal and motor responses take longer to develop and that their development is, perhaps, supported by perceptual representations in ventral-temporal cortex. An interesting speculation is that functional connections among dorsal stream and motor regions with primary visual regions (as opposed to visual perceptual regions in ventral-temporal cortex) may support early learning stages to, first, guide copying movements. The written forms produced by the copying would help to develop visual perceptual representations in ventral-temporal cortex independently of the functional communication among primary visual, dorsal stream, and motor brain regions that is guiding the motor movements. Once visual perceptual representations have been established, however, they would be integrated into the functional network that supports letter production until visual-perceptual, visual-motor, and motor processes are all over-learned at which time they begin to function relatively autonomously. There is some support for this speculation: Activity in primary visual cortex is associated with the early stages of visual perceptual learning but not later stages (Yotsumoto, Watanabe, & Sasaki, 2008) and greater functional connectivity among regions within the ventral visual stream has been associated with later stages of visual perceptual learning (Kang et al., 2018).

Functional Connectivity as a Developmental Mechanism

The results of the experiments reported in this dissertation have implications for our understanding of brain development from sensorimotor experiences. They suggest that changes in

functional connectivity after sensorimotor experiences are transient responses that are greatest during the early stages of learning and after recent training experiences. They also suggest that functional connectivity may be contributing to the development some other neural mechanism that supports the development of perceptual processes.

Functional connectivity as a transient phenomenon. Several prior works have demonstrated that training-induced changes in functional connectivity are transient, often not lasting longer than a few days (Berns et al., 2013; Ma et al., 2011). These prior works have suggested that functional connectivity during a task is greatest during the early stages of learning to perform that task (Basset et al., 2015; Sun et al., 2006) and that if training ceases at any point, functional connectivity while performing that task will decrease monotonically (Berns et al., 2013) with no loss in ability to perform the task (Phillip & Frey, 2016). Below, I discuss how these prior works can help to explain the results reported in this dissertation.

The emergence of visual-motor functional connectivity during letter perception may be characteristic of the early stages of letter learning and not later stages. This would explain why we did not find functional connectivity during literate letter perception (Chapter 4)—because any learning that might be occurring in literate adults would be considered to be in very advanced stages. It would also be consistent with the findings that functional connectivity supported letter perception in preliterate children (Chapter 2) and novel symbol perception in literate adults (Chapter 6) after production training. It would have been ideal to measure functional connectivity during letter perception in younger children who were just learning to recognize letters and in older children at a later stage of letter learning to determine if functional connectivity is characteristic of early learning, specifically, or simply related to recent training experience that occurred in the experiments, or both.

It is unlikely, however, that the emergence of visual-motor functional connectivity during letter perception is reliant upon recent sensorimotor experience with letters alone. Note that the experimental design that was used to test for functional connectivity during letter perception in literate adults included letter production within the same functional run as letter perception. If recent training with letter production increases functional connectivity during letter perception, then we should have expected to see

functional connectivity in this experimental design because they produced letters just before perceiving them. The letters produced were, furthermore, the exact same letters that were perceived, ruling out any instance-based accounts of functional connectivity. This result, an apparent absence of functional connectivity during letter perception in literate adults after recent letter production experience, suggests that functional connectivity during perception is not likely to be driven by an absence of recent sensorimotor experience with letters alone. The presence of functional connectivity during letter perception may, therefore, be related to an interaction between early learning and recent sensorimotor experience with letters.

The findings of the experiments described in this dissertation are, therefore, supportive of the notion that training-induced changes in functional connectivity are transient phenomena. They are temporary responses to particular experiences that are more strongly affected by novel circumstances. The temporary response appears to be strongly associated with the sensory and motor experiences associated with the novel circumstance. Chapter 6 reports changes in functional connectivity among visual and motor brain regions after training with different pairings of visual and motor experiences of letters. This supports the notion that experiences leave behind a residue of reverberating neural activity that is closely associated with the reverberations that supported the experience and that gradually decrease as time passes (Hebb, 1949; Alvarez & Squire, 1994).

Consistent functional connectivity patterns arise from environmental consistencies. If functional connectivity is, indeed, a transient phenomenon, then how can we explain the findings that several intrinsic functional networks are consistently found across participants and imaging sessions, even without common training manipulations (Damoiseaux et al., 2006)? Neural development is often approached as a process of building—experiences contribute to the establishment of stable functional neural networks. It would be expected, from this viewpoint, that a functional network associated with learning through experiences that couple sensory and motor systems would be well-established and stable by adulthood given our immense amount of experience with sensory-motor contingencies. The results reported in this dissertation demonstrate, contrary to what would be expected from that viewpoint, that a

short amount of training that violates learned contingencies is enough to change functional networks that would certainly have been expected to have been well-established and stable in adults (Chapter 6). I suggest that these results indicate that functional networks are not built over time but, rather, that they are *maintained* over time. The continued functioning of such sensorimotor functional networks relies on continually experiencing these sensorimotor contingencies. Intrinsic functional networks that are consistently found are, therefore, not established in the literal, physical sense, but temporary responses to reliable and consistent phenomena that most people experience (e.g., visual-motor contingency). Sensorimotor experiences would, therefore, contribute to the maintenance of a sensorimotor network that is ever-present and that supports behaviors that feed back into a relatively autonomous visual-perceptual system.

Objects contribute to consistency. As mentioned above, the results reported in this dissertation are consistent with prior works concerning the transient nature of training-induced functional connectivity: functional connectivity is greatest early in learning and decreases monotonically after training ceases (Bassett et al., 2015; Berns, et al., 2013). This dissertation adds, however, that this relationship between functional connectivity and learning holds for functional connectivity during a task that was not specifically trained (Chapter 6). The task was, specifically, the visual perception of an object that had been learned through a sensorimotor experience (Chapter 6). The results reported in Chapter 6, therefore, paint an interesting picture of the role of object perception in maintaining functional networks over time.

Objects may invoke prior sensorimotor experiences with an object, provided the object is novel in some respect and that the experience with it is recent enough. The object, in having this effect, would contribute to the ongoing maintenance of a functional network that would have faded earlier if it had not been re-stimulated. An object would, therefore, work as a vestige, of sorts, of a pattern of functional connectivity that is particularly conducive to learning. The object stores the learner's history with it, in a way, and upon being perceived, reminds the learner how interact with objects in a way that leads to better learning and, in turn, more adaptive behaviors. This idea is similar to theories of neural simulation

(Rizolatti & Craighero, 2004) but, unlike neural simulation theories, the re-invocation of prior sensorimotor experiences of an object is not necessarily related to recognition of the object (Chapter 4; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996) or to activity that simply does not reach the threshold for overt motor movement (Grèzes Tucker, Armony, Ellis, & Passingham, 2003) but, rather, it is related to making certain actions more likely than others, particularly actions that are conducive to perceptual learning.

Objects may be particularly important to the maintenance of these so-called 'learning networks' in the early stages of learning, especially if the learning that is occurring early on is actually a learning of the sensorimotor contingencies surrounding the object and not a learning of the object itself. It may be that we must first understand that sensorimotor contingencies that frame an object's existence before we can 'see' the object as an entity. In adults, such things are well-established and 'expected'. Adults have certain expectations about sensorimotor contingencies whether or not they 'know' an object and, accordingly, most objects are known well-enough to contribute to ongoing neural activity associated with those contingencies. If this were the case, then ongoing patterns of intrinsic connectivity should have implications for predispositions to learn. There is some evidence for this: intrinsic functional connectivity before learning to perform a perceptual discrimination task predicts learning rate (Baldassarre et al., 2012). Functional connectivity may, therefore, be more related to the propensity to learn given a history of consistently re-internalizing the environmental consistencies that are tied to objects within that environment.

In this dissertation, the consistent phenomenon was spatiotemporal contingency between the visual and motor experiences of a letter during letter production. Future work might explore the effects of violating other phenomena that are ubiquitous realities of human behavior. A nice place to start may be to explore interactions among the motor system and sensory systems other than the visual system. Manually exploring objects to learn about sounds they make, for instance, leads to a reactivation of the motor system when the learner simply hears those object-specific sounds again (James & Bose, 2011). Self-generated actions have specific perceptual consequences, whether they are in the visual, auditory, or

tactile sensory domains, that are linked to the action in time. As this linking seems to be important for the visual-motor functional connectivity observed in this dissertation, I would expect that the linking among actions and their auditory and tactile sensory inputs would result in similar auditory-motor and tactile-motor functional connections during learning. Another approach would be to explore interactions among sensory systems themselves in passive paradigms, such as audio-visual training paradigms.

Future Directions

This dissertation has taken the first steps in understanding the relationship among learning tasks (i.e., letter production), the functional connections that support them, and how those functional networks are related to perceptual learning (i.e., letter perception). I will conclude by discussing two potential avenues for future investigations into the relationship between functional connectivity and visual perceptual learning.

Development of functional connectivity during letter production and perception. It will be important to measure functional connectivity during letter production and letter perception in young early-literate children and literate children. This information would provide evidence in support of the proposition that visual-perceptual regions in ventral-temporal cortex are integrated into a somatomotor functional network that supports letter production before the establishment of perceptual representations. We speculated in Chapter 5 that letter production in early learning may be supported by a functional network comprised of a fronto-parietal functional network and primary visual cortex to guide what is essentially a copying of a written form. This functional network continually presents the visual-perceptual system with category exemplars from which it learns. Over time, visual-perceptual representations may be integrated into the functional network that supported earlier learning stages and, from then on, provide perceptual guidance to motor cortex, evoking a new dynamic in the functional network supporting letter perception. It is hard to know if functional connectivity during letter perception would always be absent in early learning after perceptual representations have been established, or if functional connectivity helps to refine the motor plan and somatomotor guidance for a while before ventral-temporal and motor cortices, again, begin to function relatively autonomously.

Measuring functional connectivity during letter perception in a cross-sectional design is, however, methodologically difficult (Power et al., 2012; Satterthwaite et al., 2012; Van Dijk et al., 2012). Understanding the development of functional connectivity during letter production and perception will likely require an individual differences approach that carefully controls for age.

Functional connectivity during successful and unsuccessful recognition. Another important follow-up study would be to investigate the patterns of functional connectivity *during* recognition. Chapter 6 demonstrated that symbol production led to changes in the functional network supporting symbol perception and concurrent changes in symbol recognition that persisted after the functional network dissipated. I assumed that participants were automatically recognizing the symbols during fMRI scanning and that the degree to which this happened could be characterized by an out-of-scanner recognition task. To determine whether or not functional connections support letter recognition processes, specifically, in the early stages of learning, functional connectivity must be measured during successful and unsuccessful recognition of novel symbols after training.

Final Conclusion

This research suggests that actions that tightly couple visual and motor systems are supported by functional connections that mold the neural mechanisms underlying object recognition. This work makes several contributions to our understanding of the effects of sensorimotor learning activities on brain functioning and the role of these changes in perceptual learning. They suggest several interesting avenues for follow-up work to better understand the role of these functional connections in learning.

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APPENDIX A:

MOTION ANALYSIS

Functional connectivity studies may be especially susceptible to artifacts produced by head motion, even after standard motion correction techniques are applied. Although functional connectivity estimates from gPPI analyses are considered more robust to motion-related artifacts than standard functional connectivity estimates, for the reasons stated in the methods section, we followed the functional connectivity analysis with a motion analysis to document the amount of motion present in our sample and to ensure that motion had not driven the results of the functional connectivity analysis. We based our motion analysis on the framewise displacement (FD) statistic, which is a measure of the absolute displacement of the head between sequential images (Power et al., 2012).

Different variants of the equation used to calculate the FD statistic exist. Yan et al. (2013) directly compared each of these equations and determined that the variant proposed by Jenkinson, Bannister, Brady, and Smith (2002) is most consistent, with the variant proposed by Power et al. (2012) following closely behind. However, the Jenkinson et al. (2002) model requires the assumption that the average distance between the center of the brain and cortex is 80 mm. Given that our sample consists of 5 year old child brains, images of which were normalized to an atlas of an elderly woman (Talairach & Tournoux, 1988), we turned to the variant proposed in Power et al. (2012). The Power et al. (2012) equation for the FD statistic overestimates the degree of motion and is not considered to be a conservative estimate of motion (Yan et al., 2013). Therefore, we chose to calculate the FD statistic as described in Power et al. (2012), because its assumptions are more plausible for our sample and would ensure that our motion analysis would not *underestimate* the amount of motion present in the sample.

Methods

FD time courses were constructed by summing the absolute value of the difference between time *n* and time *n-1* for each of the rigid body motion parameters (Power et al., 2012; Power et al., 2014). Summary FD scores were obtained for each subject by averaging FD scores within individual subjects

across time to summarize subject-specific motion and for conditions by averaging FD scores within task conditions across time to summarize condition-specific motion.

Subject-specific summary FD

Subject-specific summary FD (sFD) scores allowed us to select a sub-sample of individuals with the lowest sFD that included only individuals below the median sFD. We reran the gPPI analysis on these individuals and compared these results to the results obtained in the full sample. If the results held with the low-sFD subsample, then our results were not likely to have been driven by motion artifacts due to the inclusion of high-sFD. Additionally, an ANCOVA was performed to directly compare results from the low-sFD group to those of the high-sFD group for the contrasts of interest. This analysis directly assessed the degree to which the results from the low-sFD group differed from those of the high-sFD group. A difference between low- and high-sFD groups would be evidence that high-sFD subjects drove the effects in the functional connectivity analysis.

Condition-specific summary FD

Condition-specific summary FD (cFD) scores were subjected to a One-Way ANOVA to determine if motion was significantly different in one condition compared to another across subjects. A difference between conditions in cFD would be evidence that task-correlated motion drove the effects in the functional connectivity analysis. We had no a priori reason to believe motion would differ across conditions, because every task required subjects to remain still while passively viewing visual stimuli. However, we wanted to be sure that children were not moving more, by chance during a particular condition than during others.

Results

The median sFD was 0.1977 mm and scores ranged from 0.0601 mm to 1.3905 mm. Subjects were grouped based on a median split of sFD. After separating the data into low- and high-FD subsamples, we first ran the full gPPI analysis low-FD participants. Compared with the analysis on the full sample, analysis on the low-FD subsample produced very similar results. With the exception of one cluster, the same set of significant clusters were found with both analyses using the same correction for

multiple testing. This was despite the reduced sample size (N=4) of the low-FD analysis. Therefore, our results are not likely to have been driven by the inclusion of high-FD subjects introducing motion artifacts into the group results. Secondly, we added a sFD group variable to the gPPI design matrix to directly compare the strength of the interactions between low- and high-FD groups of participants. The results of this analysis were the same as the original gPPI and the interaction of the groups with the contrasts of interest did not reach significance even at p_{vox} <.001, uncorrected. This was further evidence that movement artifacts present in the high-FD participants did not artificially induce the experience-based effects in functional connectivity observed in the full sample. Finally, differences in the cFD did not reach significance ($F(7, 136) = 1.15$, $p = 0.34$), demonstrating that differing amounts of movement during specific conditions could not explain differences in functional connectivity between conditions.

Conclusion

Thus, we have demonstrated that our data are suitable for the gPPI functional connectivity analysis and have taken several steps to account for motion. We have demonstrated that a re-analysis with the lowest motion subjects produced the same results as with the full sample, which strongly indicates that these results were not driven by the presence of high-motion subjects. We have, furthermore, demonstrated that the motion between conditions was not significantly different, indicating that these results were not driven by the presence of task-correlated motion.

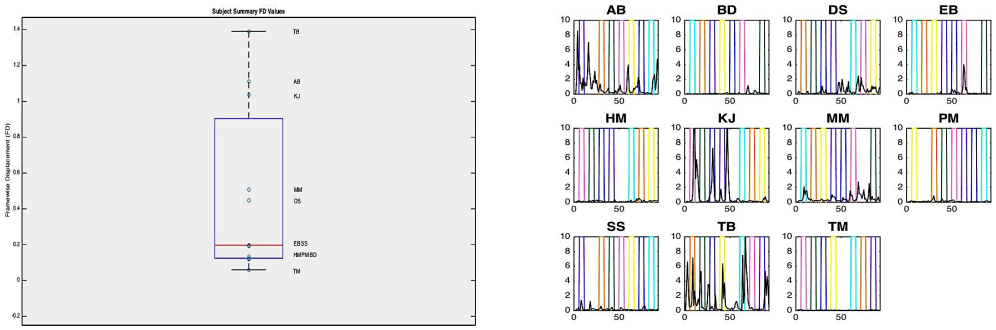

Figure S1. Motion Analysis Results for Subject-Specific FD Scores. Subjects below the median were selected as a low-motion sub-sample. Subject initials are reported, because this is the reporting style used in James and Engelhardt (2012) and, thus, allows the reader to reference the behavioral scores reported therein.

APPENDIX B:

MOTION ANALYSIS

The frame-wise displacement (FD) statistic as described in Power et al. (2012) was constructed from the rigid-body motion parameters for each run and used as a summary measure of motion over time. To determine the magnitude of task-correlated head motion, we calculated a condition-specific FD (cFD) summary score by averaging the FD score across all time points in each condition across subjects. These scores were subjected to a One-Way ANOVA to determine whether or not head motion differed significantly across participants and/or across conditions. If we find that cFD differed significantly across conditions, particularly between conditions in our primary contrasts of interest, then we would have reason to be cautious in interpreting our results.

While the FD statistic can measure head movement, it does not account for the effects of motions that may occur outside the field of view. Signal changes due to motions that occur outside the field of view are relatively minor (Barry & Menon, 2005; Jezzard & Clare, 1999). We, nonetheless, wanted to be certain that task- correlated motion, due to head movements inside the field of view or arm movements outside the field of view, did not affect our results.

Methods

To determine whether or not task-correlated arm movements affected the signal, we averaged the signal magnitude time courses from all voxels (Van Dijk et al., 2012; Power et al., 2014). This averaged time course was calculated from the BOLD signal directly, as opposed to the rigid-body motion parameters, and represented the average change in signal magnitude over time. It was, therefore, a measure of the effect of task-correlated arm movement on the BOLD signal that was independent from the FD statistic. We took the derivative of the resulting time course to create a time course the represented the rate of change of the global signal at each time point. Condition-specific summary scores of the derivative of the global mean signal (cDGM) were obtained by averaging the DGM time course across all time points in each condition across all runs. These scores were subjected to a One-Way ANOVA to determine whether or not the task-correlated arm movements affected the signal. If we find that cDGM

did differ significantly across conditions, particularly between conditions in our primary contrasts of interest, then we would have reason to be cautious in interpreting our results.

Results

Condition-specific FD scores

Condition-specific FD (cFD) scores ranged from 1.12 to 2.14, $M = 1.50$, $SD = 0.29$ (see Figure). The median cFD score was 1.66. Differences in cFD did not reach significance as determined by a One-Way ANOVA ($F(4, 270) = 1.41$, $p = 0.23$).

Condition-specific DGM scores

Condition-specific DGM (cDGM) scores ranged from 4.48 to 6.08, $M = 5.41$, $SD = 0.67$ (see Figure). The median cDGM score was 5.63. A One-Way ANOVA indicated a significant difference between conditions ($F(4, 270) = 2.65$, $p = .03$). A Tukey HSD post-hoc test revealed that cDGM during Write Without Ink ($M = 6.08$, $SD = 2.64$) was significantly greater than cDGM during Watch Static ($M = 4.48$, $SD = 1.92$), $p = 0.05$, with a 95% confidence interval of [0.02, 3.17]. No other comparisons reached significance.

Conclusion

We found no difference in cFD among conditions and only one difference in cDGM. We found that cDGM was greater during Write Without Ink than during Watch Static. Our main analyses never directly compared these Write Without Ink and Watch Static, however. We have, therefore, demonstrated that task-correlated motion between conditions did not affect the signal in some conditions more than others in our contrasts of interest, indicating that these results were not driven by the presence of task-correlated motion.

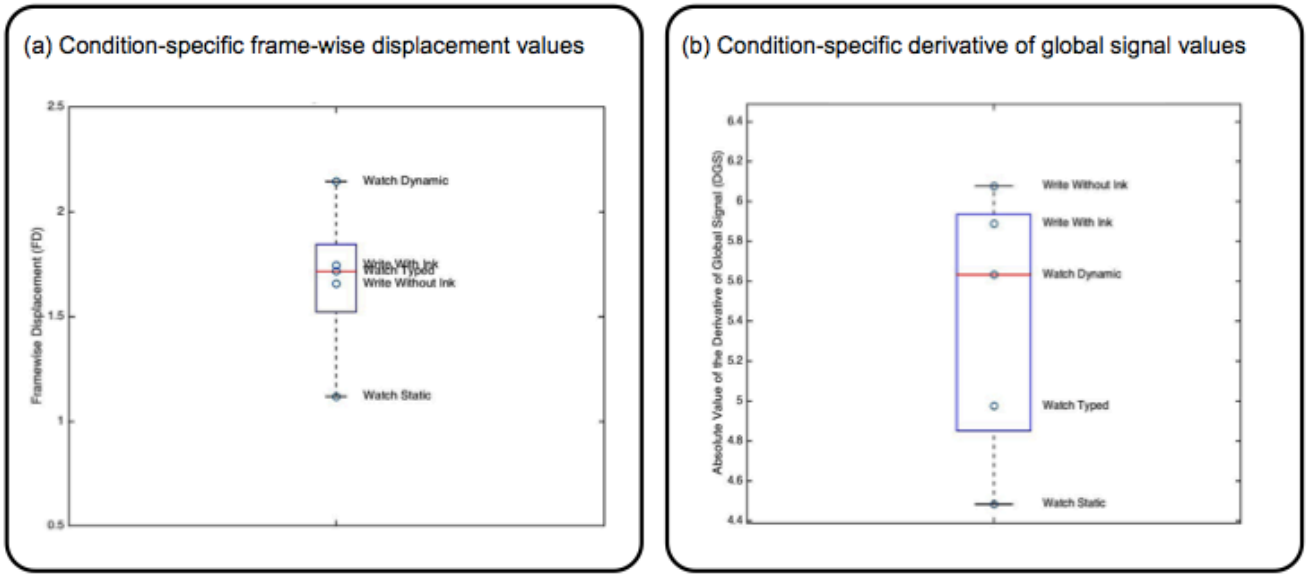

Figure S2. Motion analyses Results for Condition-Specific FD and cDGM scores. (a) Condition-specific frame-wise displacement values: Differences in cFD between conditions did not reach significance as determined by a One-Way ANOVA ($F(4, 270) = 1.41$, $p = 0.23$). (b) Differences in cDGM between conditions indicated a significant difference between conditions as determined by a One-Way ANOVA ($F(4, 270) = 2.65$, $p = .03$). A Tukey HSD post-hoc test revealed that cDGM during Draw Without Ink (M = 6.08, SD = 2.64) was significantly greater than cDGM during Watch Static (M = 4.48, SD = 1. No other comparisons reached significance.

APPENDIX C:

COMMUNITY ASSIGNMENTS FOR ROIS IN OPTIMIZED PARTITION

Optimized Partition		Left Hemisphere	Right Hemisphere
1		Left Anterior Cingulate (5) Left Anterior Cingulate (5) Left Anterior Cingulate (5) Left Anterior Cingulate (5) Left Declive (14) Left Fusiform Gyrus (14) Left Fusiform Gyrus (14) Left Inferior Frontal Gyrus (14) Left Inferior Occipital Gyrus (14) Left Inferior Temporal Gyrus (14) Left Lingual Gyrus (14) Left Medial Frontal Gyrus (5) Left Middle Temporal Gyrus (14) Left Parahippocampal Gyrus (14) Left Parahippocampal Gyrus (14) Left Uncus (14)	Right Anterior Cingulate (5) Right Culmen (14) Right Fusiform Gyrus (14) Right Inferior Frontal Gyrus (14) Right Inferior Occipital Gyrus (14) Right Inferior Temporal Gyrus (14) Right Lingual Gyrus (14) Right Lingual Gyrus (14) Right Medial Frontal Gyrus (5) Right Medial Frontal Gyrus (5) Right Medial Frontal Gyrus (5) Right Middle Temporal Gyrus (14) Right Middle Temporal Gyrus (14) Right Rectal Gyrus (14) Right Uncus (14) Right Uvula (14) Right Uvula (14)
2		Left Inferior Parietal Lobule (8) Left Middle Frontal Gyrus (8)	Right Fusiform Gyrus (14) Right Inferior Frontal Gyrus (8) Right Inferior Parietal Lobule (8) Right Inferior Parietal Lobule (8) Right Middle Frontal Gyrus (14) Right Middle Frontal Gyrus (8) Right Middle Frontal Gyrus (8) Right Middle Frontal Gyrus (8) Right Middle Frontal Gyrus (8) Right Middle Frontal Gyrus (8) Right Middle Frontal Gyrus (8) Right Middle Temporal Gyrus (8) Right Precentral Gyrus (8)
3		Left Lentiform Nucleus (10) Left Lentiform Nucleus (10) Left Lentiform Nucleus (10) Left Thalamus (10) Left Thalamus (10) Left Thalamus (10)	Right Claustrum (3) Right Claustrum (3) Right Inferior Frontal Gyrus (14) Right Inferior Frontal Gyrus (9) Right Insula (9) Right Insula (9) Right Lentiform Nucleus (10) Right Lentiform Nucleus (10) Right Lentiform Nucleus (10) Right Thalamus (10) Right Thalamus (10) Right Thalamus (10)

4	Left Cingulate Gyrus (6) Left Postcentral Gyrus (1) Left Precuneus (1) Left Precuneus (12) Left Precuneus (6)	Right Cingulate Gyrus (6) Right Paracentral Lobule (9) Right Precuneus (6) Right Precuneus (6)
5	Left Cingulate Gyrus (1) Left Inferior Parietal Lobule (1) Left Inferior Parietal Lobule (1) Left Paracentral Lobule (1) Left Postcentral Gyrus (1) Left Postcentral Gyrus (1) Left Postcentral Gyrus (1) Left Postcentral Gyrus (1) Left Precentral Gyrus (1)	Right Medial Frontal Gyrus (1) Right Paracentral Lobule (1) Right Postcentral Gyrus (1) Right Postcentral Gyrus (1) Right Postcentral Gyrus (1) Right Postcentral Gyrus (1) Right Postcentral Gyrus1 Right Precentral Gyrus (1) Right Precentral Gyrus (1) Right Precentral Gyrus (1) Right Precentral Gyrus (1) Right Precentral Gyrus (1)
6	Left Cingulate Gyrus (3) Left Cingulate Gyrus (3) Left Cingulate Gyrus (9) Left Claustrum (3) Left Insula (3) Left Medial Frontal Gyrus (1) Left Paracentral Lobule (1) Left Superior Frontal Gyrus (1) Left Superior Frontal Gyrus (3) Left Superior Frontal Gyrus (3) Left Superior Temporal Gyrus (3)	Right Cingulate Gyrus (1) Right Inferior Parietal Lobule (3) Right Insula (3) Right Medial Frontal Gyrus (1) Right Medial Frontal Gyrus (1) Right Medial Frontal Gyrus (3) Right Medial Frontal Gyrus (3) Right Middle Frontal Gyrus (3)
7	Left Inferior Frontal Gyrus (8) Left Inferior Frontal Gyrus (8) Left Inferior Parietal Lobule (12) Left Inferior Parietal Lobule (8) Left Middle Frontal Gyrus (12) Left Middle Frontal Gyrus (8) Left Middle Temporal Gyrus (12) Left Middle Temporal Gyrus (12) Left Postcentral Gyrus (1) Left Precuneus (12) Left Superior Parietal Lobule (8)	Right Angular Gyrus (8) Right Inferior Parietal Lobule (8) Right Middle Frontal Gyrus (12) Right Middle Temporal Gyrus (12) Right Precuneus (12) Right Precuneus (12) Right Superior Parietal Lobule (12)
8	Left Postcentral Gyrus (2) Left Precentral Gyrus (2)	Right Insula (2) Right Insula (4) Right Insula (4) Right Lentiform Nucleus (10) Right Precentral Gyrus (2) Right Precentral Gyrus (2)
9	Left Inferior Parietal Lobule (4) Left Insula (4) Left Insula (4) Left Insula (4)	Right Postcentral Gyrus (4) Right Postcentral Gyrus (4) Right Superior Temporal Gyrus (4) Right Transverse Temporal Gyrus (4)

	Left Postcentral Gyrus (4) Left Precentral Gyrus (4) Left Superior Temporal Gyrus (4)	
10	Left Angular Gyrus (5) Left Cingulate Gyrus (5) Left Cingulate Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Middle Temporal Gyrus (5) Left Parahippocampal Gyrus (5) Left Parahippocampal Gyrus (5) Left Posterior Cingulate (5) Left Posterior Cingulate (5) Left Precuneus (5) Left Sub-Gyral (5) Left Superior Frontal Gyrus (5) Left Superior Frontal Gyrus (5) Left Superior Frontal Gyrus (5) Left Superior Frontal Gyrus (5) Left Superior Frontal Gyrus (5)	Right Inferior Frontal Gyrus (5) Right Medial Frontal Gyrus (5) Right Medial Frontal Gyrus (5) Right Middle Temporal Gyrus (5) Right Middle Temporal Gyrus (5) Right Middle Temporal Gyrus (5) Right Parahippocampal Gyrus (5) Right Posterior Cingulate (5) Right Precuneus (5) Right Precuneus (5) Right Precuneus (5) Right Superior Frontal Gyrus (5) Right Superior Frontal Gyrus (5) Right Superior Frontal Gyrus (5) Right Superior Frontal Gyrus (5) Right Superior Temporal Gyrus (5) Right Superior Temporal Gyrus (5) Right Supermarginal Gyrus (5) Right Uvula (5)
11	Left Cuneus (7) Left Cuneus (7) Left Cuneus (7) Left Cuneus (7) Left Inferior Occipital Gyrus (7) Left Inferior Occipital Gyrus (7) Left Lingual Gyrus (7) Left Lingual Gyrus (7) Left Middle Occipital Gyrus (7) Left Middle Occipital Gyrus (7) Left Middle Occipital Gyrus (7) Left Middle Occipital Gyrus (7) Left Middle Occipital Gyrus (7) Left Posterior Cingulate (7)	Right Cuneus (7) Right Cuneus (7) Right Cuneus (7) Right Cuneus (7) Right Inferior Occipital Gyrus (7) Right Inferior Temporal Gyrus (7) Right Lingual Gyrus (7) Right Lingual Gyrus (7) Right Lingual Gyrus (7) Right Middle Occipital Gyrus (7) Right Middle Occipital Gyrus (7) Right Middle Temporal Gyrus (5) Right Middle Temporal Gyrus (7) Right Parahippocampal Gryus (7) Right Posterior Cingulate (7) Right Posterior Cingulate (7) Right Precuneus (7) Right Precuneus (7)
12	Left Anterior Cingulate (9) Left Cingulate Gyrus (9) Left Inferior Frontal Gyrus (11) Left Inferior Frontal Gyrus (14) Left Inferior Frontal Gyrus (5)	Right Anterior Cingulate (5) Right Anterior Cingulate (9) Right Cingulate Gyrus (9) Right Inferior Frontal Gyrus (9) Right Inferior Frontal Gyrus (11)

		Left Insula (9) Left Medial Frontal Gyrus (5) Left Medial Frontal Gyrus (8) Left Middle Frontal Gyrus (5) Left Middle Frontal Gyrus (8) Left Middle Frontal Gyrus (8) Left Middle Frontal Gyrus (8) Left Middle Frontal Gyrus (9) Left Middle Frontal Gyrus (9) Left Sub-Gyral (8) Left Superior Frontal Gyrus (11) Left Superior Frontal Gyrus (5) Left Superior Temporal Gyrus (11) Left Superior Temporal Gyrus (11)	Right Middle Frontal Gyrus (9) Right Middle Frontal Gyrus (9) Right Middle Temporal Gyrus (11) Right Superamarginal Gyrus (5) Right Superior Frontal Gyrus (9) Right Superior Frontal Gyrus (9) Right Superior Temporal Gyrus (11) Right Superior Temporal Gyrus (11) Right Superior Temporal Gyrus (11) Right Supermarginal Gyrus (9)
13		Left Declive (13) Left Declive (13)	Right Culmen (13) Right Declive (13)

Power et al. (2011) community assignments are in parentheses beside each ROI.

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1/2015 – 6/2017	Indiana University Imaging Research Facility Graduate Student Brain Scan Credit for fMRI scanning

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AWARDS & HONORS

2015	Commendation on Doctoral Qualifying Examinations
2015	James S. McDonnell Foundation Fellowship
2014	Graduate student poster winner at the Center of Excellence for Women in Technology Conference
2011	Runner-Up for Rotary International Ambassadorial Scholarship
2009	International Experience Scholarship
2009	Margaret A. Cook Scholarship for Foreign Study
2009	Marius J. Fauré Family Scholarship for Students of French Language and Literature
2006, 2007, 2008	Commitment to Engineering Excellence Scholarship

TRAVEL AWARDS

2015, 2016, 2017, 2018	Program in Neuroscience College of Arts & Sciences Travel Award
2017, 2018, 2019	Indiana University Provost's Travel Award for Women in Science

INTELLECTUAL PROPERTY

"Electronic tablet for use in functional MRI," *US Patent Application No. 62/370, 372*, filed August 3, 2016, (Sturgeon, J., Shroyer, A., **Vinci-Booher, S.**, & James, K.H., applicants). Amended February 4, 2019.

MANUSCRIPTS IN PROGRESS

Vinci-Booher, S., & James, K.H. Visual experiences of letter production contribute to the development of the neural systems supporting letter perception. Manuscript under review.

Vinci-Booher, S., & James, K.H. Parietal involvement during visually and non-visually guided letter production. Manuscript in preparation.

Vinci-Booher, S., Nikoulina, A., James, T.W., & James, K.H. Visual-motor contingency during symbol production contributes to the development of the neural systems supporting symbol perception and concurrent gains in symbol recognition. Manuscript in preparation.

Vinci-Booher, S., Sehgal, N., & James, K.H. Visual and motor experiences of handwriting result in visual recognition gains. Manuscript in preparation.

Vinci-Booher, S., & James, K.H. The development of the neural systems supporting letter production. Manuscript in preparation.

JOURNAL PUBLICATIONS

Vinci-Booher, S., Cheng, H., & James, K.H. (2019). An analysis of the brain systems involved with producing letters by hand. *Journal of Cognitive Neuroscience, 31*(1), 138-154.

Vinci-Booher, S., Sturgeon, J., James, T., & James, K.H. (2018). The MRItab: An MR-compatible touchscreen with video-display. *Journal of Neuroscience Methods,* 306, 10-18.

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Vinci-Booher, S., James, T. W., & James, K. H. (2016). Visual-motor functional connectivity in preschool children emerges after handwriting experience. *Trends in Neuroscience and Education*, *5*(3), 107-120.

Vinci-Booher, S., & James, K. H. (2016). Neural substrates of sensorimotor processes: Letter writing and letter perception. *Journal of Neurophysiology, 115*(1), 1-4.

Foroud, T., Wetherill, L., **Vinci-Booher, S.**, Moore, E.S., Ward, R.E., Hoyme, H.E., et al. (2012). Relation over time between facial measurements and cognitive outcomes in alcohol exposed children. *Alcoholism: Clinical & Experimental Research,* 36(9), 1634-1646.

Anthony, B., **Vinci-Booher, S.**, Wetherill, L., Ward, R.E., Goodlett, C., & Zhou, F.C. (2010). Alcohol induced facial dysmorphology in C57BL/6 mouse models of fetal alcohol spectrum disorder. *Alcohol,* 44(7-8), 659-671.

BOOK CHAPTERS

James, K.H., **Vinci-Booher, S.**, & Muñoz-Rubke, F. (2017). The impact of multimodal-multisensory learning on human performance and brain activation patterns. In S. Oviatt, B. Schuller, & Cohen, P. (Eds.), *Handbook of Multimodal-Multisensor Interfaces*. San Rafael, CA: Morgan & Claypool Publishers.

CONFERENCE PROCEEDINGS PUBLICATIONS

Fang, S., Liu, Y., Huang, J., **Vinci-Booher, S.**, Anthony, B., & Zhou, F.C. (2010). Surface feature analysis using video volumes of mouse embryos for fetal alcohol syndrome classification. *International Conference on Digital Image Computing: Techniques and Applications* (pp. 22-26). Sydney, Australia: Institute of Electrical and Electronics Engineers. (57% acceptance rate).

Fang, S., Liu, Y., Huang, J., **Vinci-Booher, S.**, Anthony, B., & Zhou, F.C. (2009). Facial image classification of mouse embryos for the animal model of fetal alcohol syndrome. *Symposium on Applied Computing* (852-856). Hawaii: Association for Computing Machinery. (29% acceptance rate).

Belcher, C., Terry, M., **Vinci-Booher, S.**, & Du, Y. (2007). Video image based multimodal face recognition system. *Illinois-Indiana Section Conference* (paper 14-1-10). Indiana: American Society for Engineering Education.

ORAL PRESENTATIONS

James, K.H., & **Vinci-Booher, S.** (2019, May). Visual Experiences During Letter Production Contribute to the Development of the Neural Systems Supporting Letter Perception. In T. Schubert, *Reading as a visual act: Recognition of visual letter symbols in the mind and brain.* Symposium to be conducted at the Annual Meeting of the Vision Sciences Society, St. Pete Beach, FL, USA.

Vinci-Booher, S., Nikoulina, A., James, T.W., & James, K.H. (2019, March). Sensorimotor Contingency Leads to Developmental Changes in the Neural Mechanisms Supporting Visual Recognition. Data blitz presented at the Annual Meeting of the Cognitive Neuroscience Society, San Francisco, CA, USA.

Vinci-Booher, S., & James, K.H. (2017, October). The Developmental Trajectory of Brain Systems Supporting Handwriting and the Perception of Handwritten Letters. Oral presentation at the Neuroscience Seminar at Loyola University, Chicago, IL.
(Invited talk.)

James, K.H., & **Vinci-Booher, S.** (2017, October). The Development of the Neural Systems that Support Production and Perception of Handwritten Forms. In B.I. Bertenthal & J.J. Lockman, *Mind in motion: The development of cognitive processes in real time.* Symposium conducted at the Cognitive Development Society Biennial Conference, Portland, OR, USA.

Vinci-Booher, S., & James, K.H. (2016, October). Brain Systems Supporting Handwriting and Letter Perception Across Development. Oral presentation at the Psychological and Brain Sciences Alumni Homecoming & Award Banquet at Indiana University, Bloomington, IN, USA.
(Invited talk.)

Vinci-Booher, S., James, T.W., & James, K.H. (2015, March). The Influence of Visual-Motor Experiences on the Development of Brain Mechanisms Subserving Letter Perception. In E. Wakefield & M. Novack, *Comparing the effects of active and passive learning experiences through action and gesture.* Symposium conducted at the Biennial Meeting of the Society for Research in Child Development**,** Philadelphia, PA, USA.

CONFERENCE POSTER PRESENTATIONS & ABSTRACTS

Vinci-Booher, S., Nikoulina, A., James, T.W., & James, K.H. (2019, March). *Sensorimotor contingency leads to developmental changes in the neural mechanisms supporting visual recognition.* Poster presented at the Annual Meeting of the Cognitive Neuroscience Society, San Francisco, CA, USA.

Vinci-Booher, S., Sehgal, N., & James, K.H. (2018, May). *Visual and motor experiences of handwriting contribute to gains in visual recognition*. Poster presented at the Annual Meeting of the Vision Sciences Society, St. Pete Beach, FL, USA.

DelaCuesta, C., **Vinci-Booher, S.**, & James, K.H. (2018, April). *Novel symbol learning: The maintenance of brain changes over time.* Poster presented at the Center of Excellence for Women in Technology Conference, Bloomington, IN, USA.

Harris, S., **Vinci-Booher, S.**, & James, K.H. (2018, April). *Handwriting influence on symbol learning in adults.* Poster presented at the Center of Excellence for Women in Technology Conference, Bloomington, IN, USA.

Vinci-Booher, S., & James, K.H. (2017, October). *The development of the neural systems supporting handwriting and letter perception from kindergarten to adulthood.* Poster presented at the Cognitive Development Society Biennial Conference, Portland, OR, USA.

Yearling, E., **Vinci-Booher, S.**, & James, K.H. (2017, April). *Investigating changes in functional connectivity between visual and motor systems after handwriting practice.* Poster presented at the Center of Excellence for Women in Technology Conference, Bloomington, IN, USA.

Vinci-Booher, S., Sehgal, N., Munoz-Rubke, F., & James, K.H. (2016, May). *Perceptual and motor effects of letter writing on brain regions associated with letter perception.* Poster presented at the Annual Meeting of the Vision Sciences Society, St. Pete Beach, FL, USA.

Vinci-Booher, S., Cheng, H., & James, K.H. (2016, March). *Handwriting as a visually guided action: A developmental neuroimaging study.* Poster presented at the Latin American School for Education, Cognitive, and Neural Sciences, Buenos Aires, Argentina.

Zemlock, D., **Vinci-Booher, S.**, & James, K.H. (2016, April). *Learning about letters through handwriting practice.* Poster presented at The National Conference on Undergraduate Research, Asheville, NC, USA.

Vinci-Booher, S., Engelhardt, L., James, T.W., & James, K.H. (2015, March). *Functional connections during letter perception reflect aspects of letter writing.* Poster presented at the Annual Meeting of the Cognitive Neuroscience Society, San Francisco, CA, USA.

Vinci-Booher, S., James, T.W., & James, K.H. (2015, March). *Investigating functional connectivity in the developing brain using generalized psychophysiological interactions analysis.* Poster presented at the Biennial Meeting of the Society for Research in Child Development, Philadelphia, PA, USA.

Sehgal, N., **Vinci-Booher, S.**, & James, K.H. (2015, February). *The relationship between handedness and activation in the visual cortex of the brain.* Poster presented at the Center of Excellence for Women in Technology Conference, Bloomington, IN, USA.

Vinci-Booher, S., Engelhardt, L., James, T.W., & James, K.H. (2014, March). *Investigating the development of letter perception using gPPI connectivity analysis.* Poster presented at the Center of Excellence for Women in Technology Conference, Bloomington, IN, USA.

Black, L., **Vinci-Booher, S**., Begyn, E., McDonald, B.C., Katzenstein, J. (2013, October). *Neurocognitive and behavioral profile differences in children treated for medulloblastoma.* Poster presented at the Annual Meeting of the American Academy of Clinical Neuropsychology, Chicago, IL, USA.

Highley, E., **Vinci-Booher, S.**, Begyn, E., and Katzenstein, J. (2013, June). *Evaluation of intellectual abilities pre- and post- radiation therapy in preschool aged children with solid brain tumors.* Published abstract at the Annual Meeting of the American Academy of Clinical Neuropsychology, Chicago, IL, USA.

Black, L., Begyn, E., McDonald, B., **Vinci-Booher, S.**, Katzenstein, J. (2013, June) *Neuropsychological outcomes in children with medulloblastoma.* Published abstract at the Annual Meeting of the American Academy of Clinical Neuropsychology, Chicago, IL, USA.

Black, L., Begyn, E., McDonald, B., **Vinci-Booher, S**., Katzenstein, J. (2013, June) *Behavioral outcomes in children with medulloblastoma.* Published abstract at the Annual Meeting of the American Academy of Clinical Neuropsychology, Chicago, IL, USA.

Anthony, B., **Vinci-Booher, S.,** Veene, B., Wetherill, L., Goodlett, C., Ward, R., & Zhou, F. C. (2012, June). *Effects of duration and dose of prenatal alcohol exposure via maternal liquid diet on facial dysmorphology in C57BL/6J mice.* Symposium conducted at the 35th Annual Scientific Meeting of the Research Society on Alcoholism, San Francisco, CA, USA.

Wetherill, L., **Vinci-Booher, S.,** Mattson, S., Coles, C., Sowell, E., McCarthy, N., ... & Foroud, T. (2012, June). *Gene x alcohol exposure: what does this interaction tell us about phenotypic variation in*

fetal alcohol spectrum disorders? Symposium conducted at the 35th Annual Scientific Meeting of the Research Society on Alcoholism, San Francisco, CA, USA.

Fang, S., Liu, Y., Huang, J., **Vinci-Booher, S.**, Anthony, B., & Zhou, F.C. (2010, June). *Surface analysis from video volumes for fetal alcohol syndrome classification.* Poster presented at the International Conference on 3D Data Processing, Visualization, and Transmission, Sydney, Australia.

Anthony, B., **Vinci-Booher, S.**, Wetherill, L., Ward, R., Goodlett, C., & Zhou, F.C. (2009, June). *Alcohol induced facial dysmorphology in C57BL/6 mouse models of Fetal Alcohol Spectrum Disorder.* Poster presented at the Research Society on Alcoholism meeting, San Diego, CA, USA.

Belcher, C., Terry, M., **Vinci-Booher, S.**, & Du, Y. (2006, October). *Multimodal face recognition system.* Poster presented at the Indiana University Undergraduate Research Conference, Indianapolis, IN, USA.

TEACHING EXPERIENCE

Courses

Summer 2016, 2017, 2018	Instructor, *Trigonometry I (2-week course)* Foundations in Science and Mathematics Summer Program for High School Students, College of the Arts & Sciences, Indiana University, Bloomington, Indiana
Fall 2016	Lab Instructor, *P211: Methods of Experimental Psychology* Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana
Summer 2012	Instructor, *English as a Second-Language (1-week course)* Saint Nicolas Parish High School, Môle Saint-Nicolas, Haïti

Trainees

1/2018 – 5/2018	Sarah Harris, Capstone Student The Contribution of Visual and Motor Experiences to Symbol Learning
6/2017 – 7/2017	Amanda Ellison, Groups STEM Summer Research Experience Student Digital Analysis of Letters Handwritten by Early-literate Children
6/2016 – 5/2017	Neha Sehgal, Honors Thesis Student The Role of Dynamic Representations in Symbol Learning
8/2016 – 12/2016	Chandler Boys, Capstone Student Developing a Handwriting Training Paradigm for Early-literate Children
8/2016 – 12/2016	Emily Yearling, Capstone Student Preprocessing of fMRI Data from Child Participants
6/2015 – 8/2016	Debby Zemlock, Honors Thesis Student Learning About Letters Through Handwriting
6/2015 – 7/2015	Tayla Frizzell, Summer Research Experience for Undergraduates Student Automated Identification and Scoring of Child Handwriting Samples

DEPARTMENT, COLLEGE, & UNIVERSITY SERVICE

2019 – *present*	Conversations in Science at IU (http://blogs.iu.edu/sciu/)
2015 – *present*	Indiana University Groups STEM Mentor, Bloomington, Indiana
2015 – *present*	Foundations in Science & Mathematics at IU, Math Course Committee
2015 – *present*	Preparing Future Faculty Conference Planning Committee at IU
2018	Graduate Student Coordinator for APS Learning Workshop at IU
2017	Emerging Areas of Research Faculty Search Committee at IU
2012 – 2013	Transportation Committee at IUPUI
2009	Hosted the Society of Women Engineers Region H Conference at IUPUI
2006 – 2009	Society of Women Engineers (SWE) Fundraising Committee at IUPUI

AD HOC REVIEWER SERVICE

Brain Imaging & Behavior, Educational Psychology Review, Reading & Writing, Investigative Ophthalmology and Vision Science

PROFESSIONAL ORGANIZATIONS

2017 – *present*	Cognitive Development Society
2015 – *present*	Vision Sciences Society
2014 – *present*	Cognitive Neuroscience Society
2014 – 2015	Society for Research in Child Development
2005 – 2009	Society of Women Engineers